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One-pot synthesis of phenols from aromatic aldehydes by Baeyer–Villiger oxidation with H_2O_2 using water-tolerant Lewis acids in molecular sieves

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Abstract

Sn-Beta zeolite is employed as catalyst in the Baeyer–Villiger oxidation of aromatic aldehydes. Aldehydes involving alkoxy substituents are oxidized to the corresponding formate ester which are hydrolyzed to the corresponding phenols. Choosing the adequate reaction conditions the main product can be preselected. Dioxane solvent and a hydrogen peroxide deficit give predominantly the ester whereas ethanol solvent or aqueous acetonitrile favor the phenol product. Double bonds in alkyl side chains do not react and the corresponding unsaturated phenols are obtained with very high chemoselectivity. Brønsted sites are active for the Baeyer–Villiger oxidation of aromatic aldehydes with H_2O_2 provided that the molecule does not contain olefinic groups. In any case, the selectivity of Brønsted acid zeolites is lower than that of Sn-Beta.

Keywords: Oxidation aromatic aldehydes; Baeyer–Villiger oxidation aldehydes; Baeyer–Villiger oxidation with hydrogen peroxide; Sn-Beta Lewis acid catalyst

1. Introduction

Substituted phenols, specially 4-alkoxy derivatives, are important substances in organic chemistry since they are intermediates for drugs, agrochemicals, and dyes [1]. They are useful as polymerization inhibitors for vinyl monomers and stabilizers for polyesters [1] as well as antioxidants for foods and cosmetics [2] and have been evaluated for anti-lipid-peroxidation activity in rat liver microsomes [3]. Furthermore, they have shown physiological activity. *para*-Alkoxyphenols can be employed for treating melanomas [4,5] since they deactivate the ribonucleotide reductase in tumor cells and, thereby, inhibit the growth of tumor cells [6]. This inhibition of the ribonucleotide reductase can also be applied in AIDS therapy [7].

The 4-alkoxyphenols can be prepared by monoalkylation of hydroquinone [3,4,8]. However, di-alkylation can also occur decreasing the yield of the desired substrate. An alternative synthesis of the mono-alkoxyphenols starts with the Baeyer–Villiger (BV) oxidation of aromatic aldehydes [9] which are readily prepared by the Vilsmeier–Haack method from alkoxy benzene [10]. The Baeyer–Villiger oxidation of alkoxybenzaldehydes has been extensively studied with *ortho*-, *meta*-, and *para*-anisaldehyde (methoxybenzaldehyde) as model substrate. Several oxidants such as *meta*-chloroperbenzoic acid (mCPBA) [10], monopersuccinic acid [11], H_2O_2/seleninic acid [12], H_2O_2/methanol/H_2SO_4 [13], and H_2O_2/formic acid [14] have been tested for this reaction. The percarboxylic and perseleninic acids gave good to excellent yields of the corresponding phenol for the *ortho*- and the *para*-isomer [10–12]. The *meta*-anisaldehyde is transformed into *meta*-anisic acid predominantly since the methoxy group in *meta* position does not favor the migration of the aromatic moiety. The drawback of these oxidation methods is the waste produced that in the case of the percarboxylic acids is at least one molecule of the acid, while in the case of perseleninic acid considerable amounts of catalyst are needed since within 30 h turnover numbers (TON) as low as 12 have been reported [12]. The BV oxidation with hydrogen peroxide catalyzed by sulfuric acid gives excellent yields of the desired products; however, water-free conditions and highly concentrated hydrogen peroxide were necessary since the reaction is believed to proceed via the peroxy hemiacetal [13]. The oxidation with hydrogen peroxide in formic acid is less suitable for the production of

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phenols since it has been developed for the general oxidation of aldehydes to carboxylic acids. There is then much incentive to find new environmentally friendly catalysts and processes for converting the substituted aromatic aldehydes to the corresponding phenols.

We have recently introduced Sn-Beta zeolite and Sn-MCM-41 catalysts that are active and selective using aqueous H_2O_2 as oxidant while producing only H_2O as subproduct [15–17]. We will show here that by properly coupling catalyst design and reaction conditions very high turnover numbers and selectivity to phenols can be obtained in a one-pot reaction system. It will also be shown that this is at present an excellent alternative for producing phenolic molecules with pharmaceutical interest when an unsaturated alkyl group is present.

2. Experimental

2.1. Synthesis of the catalysts

All Sn-Beta, Al-Beta, and Sn,Al-Beta zeolites with the Sn and Al contents as stated in Table 4 were synthesized according to the literature procedure [16,18]. Sn contents were determined by chemical analysis. The Beta zeolites were calcined at 853 K for 3 h. A high crystallinity of the zeolites was observed by XRD, and in the case of Sn-Beta samples no peaks of SnO_2 were found in the diffractrogram. Nitrogen adsorption experiments on the calcined Beta samples gave an isotherm very similar to that of pure silica Beta with values of micropore volume of 0.20–0.21 $cm^3\,g^{-1}$ and BET surface areas of 450–475 $m^2\,g^{-1}$. All Beta samples were used directly after calcination or after activation for 2 h at 473 K under dynamic vacuum.

2.2. In situ IR measurements

For the IR study of the interaction of the different aromatic aldehydes with active sites of zeolites, a sample of the zeolite was first treated overnight at 673 K under dynamic vacuum (1.33×10^{-3} Pa) in order to remove adsorbed H_2O. Then the corresponding aldehyde was adsorbed and the IR spectrum was recorded at room temperature. Afterward, the organic material was desorbed successively at 323, 373, and 473 K. An IR spectrum was recorded after each desorption.

2.3. Oxidations

Aldehdyes **1a** to **1i**, hydrogen peroxide (50%), *meta* chloroperbenzoic acid (77% max), and solvents were purchased from Aldrich in the highest purity available ($\geqslant 98\%$) and used without further purification. GC analyses were carried out on a HP 5890 gas chromatograph equipped with a 25-m HP-5 column. GC-MS analyses for the identification of products were carried out on an Agilent Technologies 6890N apparatus coupled with an Agilent Mass Selective Detector 5973 Network. ^{1}H NMR spectra were recorded with a Bruker spectrometer at a frequency of 300 MHz and ^{13}C spectra at a frequency of 75 MHz.

2.4. Synthesis of 4-(3-methylbut-2-enoxy)-benzaldehyde (**1j**) [19]

4-Hydroxybenzaldehyde (2.4 g, 20 mmol) and 3.27 g of 4-bromo-2-methyl-2-butene were dissolved in 60 mL dry dimethylformamide. Potassium iodide (0.16 g, 1.5 mmol) and 11 g (78 mmol) of fine powdered potassium carbonate were added and the reaction mixture was stirred for 2 h at room temperature. Water (ca. 30 mL) was added and the mixture extracted with methyl *tert*-butyl ether (4 times, 20 mL). The combined organic phases were washed with 30 mL of 10% HCl and with 30 mL of 10% aqueous K_2CO_3 solution. After drying with $MgSO_4$, the solvent was removed with a rotavaporator and 2.8 g (15 mmol, 74%) of a pale yellow liquid was obtained.

MS m/z (%): 190 (7) $[M]^+$, 121 (100), 93 (8), 77 (5), 69 (96), 53 (10), 41 (46). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): $\delta = 1.76$ (s, 3 H, 9-H or 10-H), 1.81 (s, 3 H, 9-H or 10-H), 4.63 (d, $J = 12.5$ Hz, 2 H, 6-H), 5.46 (m, 1 H, 7-H), 7.00 (d, $J = 8.7$ Hz, 2 H, 4-H), 7.83 (d, $J = 8.7$ Hz, 2 H, 3-H), 9.89 (s, 1 H, 1-H). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): $\delta =$ 194.4, 167.6, 142.7, 135.6, 122.4, 118.6, 68.8, 29.4, 21.9.

2.5. Synthesis of 4-(but-3-enoxy)-benzaldehyde (**1k**)

Following the procedure for aldehyde **1j**, 4-hydroxybenzaldehyde (1.2 g, 10 mmol), 1.4 g of 4-bromo-1-butene, 30 mL of dry dimethylformamide, potassium iodide (0.080 g, 0.75 mmol), and 5.5 g (39 mmol) of fine powdered potassium carbonate were employed. After evaporation of the solvent 0.30 g (1.7 mmol, 17%) of the desired aldehyde **1j** was obtained.

MS m/z (%): 176 (44) $[M]^+$, 164 (39), 148 (31), 135 (13), 121 (54), 110 (100), 105 (13), 93 (20), 77 (17), 65 (20), 55 (86).

2.6. Synthesis of 4-(but-3-enoxy)-benzene (**8**)

Following the procedure for aldehyde **1j**, phenol (0.96 g, 10 mmol), 1.4 g (10 mmol) of 4-bromo-1-butene, 30 mL of dry dimethylformamide, potassium iodide (0.17 g, 0.81 mmol), and 5.5 g (39 mmol) of fine powdered potassium carbonate were employed. After evaporation of the solvent the crude reaction mixture was submitted to column chromatography (4:1 mixture of hexane and tert-butyl methyl ether; $R_f = 0.8$). 0.70 g (4.31 mmol, 41%) of the desired ether **8** were obtained.

MS m/z (%): 162 (13) $[M]^+$, 147 (10), 107 (12), 94 (100), 66 (19), 55 (14). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): $\delta = 1.74$ (s, 3 H, 8-H or 9-H), 1.79 (s, 3 H, 8-H or 9-H), 4.50 (d, 2 H, 5-H), 5.50 (t, $J = 6.7$ Hz, 1 H, 6-H), 6.94 (m, 3 H, 1-H, 3-H), 8.36 (t, 2 H, 2-H). ^{13}C NMR (75 MHz, $CDCl_3$,

298 K): $\delta = 18.6$, 26.2, 65.0, 115.1, 120.2, 120.9, 129.8, 136.4, 159.2.

2.7. General procedure for the Baeyer–Villiger oxidation

The amount of 0.50 g of aldehyde, 0.30 g of 50% aqueous hydrogen peroxide, and water (if required) were dissolved in 3.0 g of the corresponding solvent (normally acetonitrile). Then 50 mg of the catalyst was added, and the reaction mixture was stirred and heated to 353 K for 7 h. The reaction was followed by gas chromatography, and the products were identified by comparison with reference samples, by GC-MS spectroscopy, or after purification by ^{1}H NMR spectroscopy.

Reaction conditions for Tables 7 and 8: 0.25 g (1.4 mmol) of aldehyde **1j** or **1k**, 0.15 g (2.3 mmol) of 50% aqueous hydrogen peroxide, 1.5 g acetonitrile, 25 mg of catalyst, and 353 K reaction temperature.

Reaction conditions for Scheme 5 and Table 9: 0.25 g (1.8 mmol) of aldehyde **1a**, 0.16 g (2.3 mmol) 50% aqueous H_2O_2 50%, 0.29 g (1.8 mmol) of ether **8**, 1.5 g of acetonitrile, and 0.025 g of catalyst.

Reaction conditions for Table 10: for the first entry, 1.0 g of aldehyde **1a**, 0.6 g of 50% aqueous hydrogen peroxide, 6.0 g of acetonitrile, 353 K, 7 h, and 100 mg of Sn-Beta; after the reaction, the catalyst was filtered out, air-dried overnight, and activated at 473 K/vacuum for 2 h as described for fresh catalyst. For entries 2–5 and 7, the amount of reagents was scaled down with respect to the catalyst amount available.

Ester **2a**, MS m/z (%): 152 (37) $[M]^+$, 124 (76), 109 (100), 81 (36), 53 (12).

Alcohol **3a**, MS m/z (%): 124 (92) $[M]^+$, 109 (100), 81 (45), 53 (16).

Acid **4a**, MS m/z (%): 152 (91) $[M]^+$, 135 (100), 122 (9), 109 (9), 107 (11), 105 (11), 91 (22), 77 (18), 63 (11).

Ester **2b**, MS m/z (%): 166 (24) $[M]^+$, 138 (25), 110 (100), 81 (15), 53 (6).

Alcohol **3b**, MS m/z (%): 138 (55) $[M]^+$, 110 (100), 81 (15), 53 (6).

Ester **2c**, MS m/z (%): 180 (49) $[M]^+$, 152 (13), 110 (100), 81 (15), 65 (7), 53 (8).

Alcohol **3c**, MS m/z (%): 152 (49) $[M]^+$, 110 (100), 81 (15), 65 (8), 53 (8).

Ester **2d**, MS m/z (%): 214 (48) $[M]^+$, 186 (100), 157 (14), 129 (12), 109 (19), 77 (25), 51 (12).

Alcohol **3d**, MS m/z (%): 186 (100) $[M]^+$, 157 (12), 129 (8), 109 (12), 77 (10), 51 (5).

Alcohol **3e**, MS m/z (%): 108 (100) $[M]^+$, 90 (21), 80 (43), 77 (60), 63 (10), 51 (22).

Acid **4e**, MS m/z (%): 136 (82) $[M]^+$, 119 (69), 91 (100), 65 (19).

Ester **2f**, MS m/z (%): 178 (17) $[M]^+$, 163 (21), 135 (100), 107 (31), 91 (12), 77 (9), 55 (8).

Alcohol **3f**, MS m/z (%): 150 (23) $[M]^+$, 135 (100), 107 (31), 95 (11), 77 (8).

Acid **4f**, MS m/z (%): 178 (19) $[M]^+$, 164 (12), 163 (100), 135 (28), 115 (8), 91 (28), 77 (12).

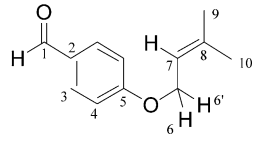
Ester **2g**, MS m/z (%): 122 (31) $[M]^+$, 94 (100), 77 (5), 66 (27), 51 (7).

Alcohol **3g**, MS m/z (%): 94 (100) $[M]^+$, 66 (30), 55 (5), 50 (5).

Acid **4g**, MS m/z (%): 122 (89) $[M]^+$, 105 (100), 77 (62), 51 (23).

2.8. Oxidation of aldehyde *1j* with mCPBA

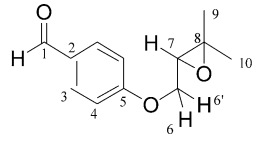
The amounts of 25 mg of aldehyde **1j** and 9 mg of mCPBA were dissolved in 150 mg of acetonitrile. After standing at room-temperature for 2 h the sample was submitted to GC and GC-MS analyses.



Ester **2j**, MS m/z (%): 206 (2) $[M]^+$, 138 (65), 110 (100), 81 (8), 69 (38), 53 (14), 41 (23).

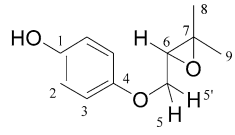
Alcohol **3j**, MS m/z (%): 178 (8), 110 (100), 81 (19), 69 (39), 53 (16).

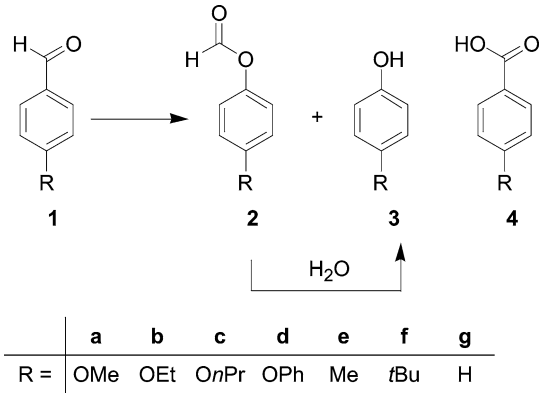
Epoxyaldehyde **5j**, MS m/z (%): 206 (67) $[M]^+$, 147 (8), 136 (22), 121 (62), 105 (21), 85 (100), 71 (30), 59 (76), 51 (14), 43 (38). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): $\delta = 1.38$ (s, 3 H, 9-H or 10-H), 1.41 (s, 3 H, 9-H or 10-H), 3.17 (dd, $J_{6,7} = 5.95$ Hz, $J_{6',7} = 5.95$ Hz, 1 H, 7-H), 4.13 (dd, $J_{6',7} = 5.95$ Hz, $J_{6',6} = 11.0$ Hz, 1 H, 6′-H), 4.25 (dd, $J_{6,7} = 5.95$ Hz, $J_{6,6'} = 11.0$ Hz, 1 H, 6-H), 7.05 (d, $J = 8.80$ Hz, 2 H, 4-H), 7.85 (d, $J = 8.80$ Hz, 2 H, 3-H), 9.89 (s, 1 H, 1-H).



Epoxyester **6j**, MS m/z (%): 222 (48) $[M]^+$, 194 (15), 138 (12), 123 (13), 110 (100), 93 (10), 85 (30), 71 (24), 65 (11), 59 (32), 43 (29).

Epoxyphenol **7j**, MS m/z (%): 194 (50) $[M]^+$, 123 (8), 110 (100), 85 (43), 59 (52), 43 (17). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): $\delta = 1.35$ (s, 3 H, 8-H or 9-H), 1.38 (s, 3 H, 8-H or 9-H), 3.17 (dd, signal overlapping partially with signals of epoxyaldehyde **5j**, 1 H, 6-H), 4.01 (dd, $J_{5',6} = 5.60$ Hz, $J_{5',5} = 10.9$ Hz, 1 H, 5-H or 5′-H), 4.07 (dd, $J_{5,6} = 5.60$ Hz, $J_{5,5'} = 10.9$ Hz, 1 H, 5-H or 5′-H), 6.76 (d, $J = 9.20$ Hz, 2 H, 2-H or 3-H), 6.82 (d, $J = 9.20$ Hz, 2 H, 2-H or 3-H).





Scheme 1.

2.9. Oxidation of aldehyde *1j* with hydrogen peroxide catalyzed by methyltrioxorhenium (MTO) in acetonitrile

The amounts of 0.50 g of aldehyde **1j** and 0.30 g of 50% aqueous hydrogen peroxide were dissolved in 3.0 g of acetonitrile. Then, 10 mg (1.56 mol%) of MTO was added, and the reaction mixture stirred and heated to 353 K for 7 h and, then analyzed by GC and GC-MS analyses.

2.10. Oxidation of aldehyde *1j* with hydrogen peroxide catalyzed by methyltrioxorhenium in methyl-tert-butyl ether

To a solution of 0.195 g of aldehyde **1j** in 1 mL of 3 M etheric solution of hydrogen peroxide 1.3 mg MTO was added. The reaction was stirred at room temperature for 7 h and then analyzed by GC and GC-MS analyses.

2.11. Oxidation of aldehyde *1k* with mCPBA

The amounts of 25 mg of aldehyde **1k** and 13 mg of mCPBA were dissolved in 155 mg of acetonitrile. After standing at room temperature for 2 h the sample was submitted to GC and GC-MS analyses.

Ester **2k**, MS m/z (%): 192 (15) $[M]^+$, 164 (24), 136 (5), 81 (9), 55 (39).

Alcohol **3k**, MS m/z (%), 164 (38) $[M]^+$, 136 (7), 110 (100), 93 (6), 81 (11), 55 (26).

3. Results and discussion

In order to design the catalyst and reaction conditions for the Baeyer–Villiger reaction of aldehydes, we selected the *para*-anisaldehyde (**1a**) as model substrate. The starting catalyst was a Sn-Beta sample (Beta-1) with 2 wt% of SnO_2 content. The reaction was performed using H_2O_2 as oxidant, acetonitrile as solvent, and 353 K reaction temperature. After 7 h reaction time the *para*-anisaldehyde conversion was 56% and the only observed products were the *para*-methoxyphenyl formate (**2a**) and *para*-methoxyphenol (**3a**, Scheme 1). In Fig. 1 the yield of reaction products versus total conversion is presented. It can be seen there that the formate ester **2a** is a primary and unstable product, whereas the phenol **3a** presents a secondary character. Indeed, product **3a** should be formed by hydrolysis of ester **2a** with the water present in the reaction media.

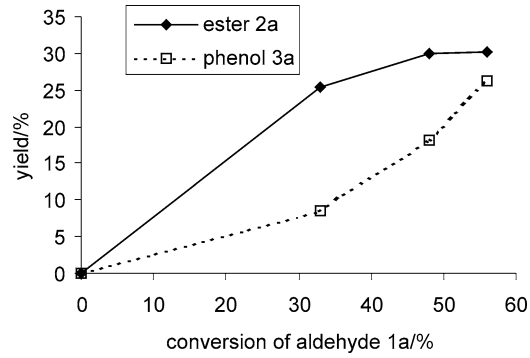


Fig. 1. Yield of ester **2a** and alcohol **3a** versus total conversion of aldehyde **1a**.

Table 1
Influence of the water amount on the hydrolysis of the ester to the alcohol

Entry	Water (mg)	TON	Conversion (%)	Product distribution		
				Ester **2a**	Alcohol **3a**	Other
1	0	317	56	54	46	0
2	20	314	57	52	48	0
3	50	295	53	39	61	0
4	100	310	56	32	68	0
5	200	350	62	18	82	0
6	300	307	54	15	85	0
7	500	327	59	4	96	0

Reaction conditions: 0.5 g of aldehyde **1a**, 0.30 g of 50% aqueous hydrogen peroxide, 3.0 g of acetonitrile, water (when indicated), and 50 mg of catalyst Beta-1 (Sn-Beta) were stirred for 7 h at 353 K.

It must be pointed out that in most of the BV oxidation of aldehydes, the desired product is the alcohol rather than the ester. However, since the alcohol is produced in a consecutive step by hydrolysis of the ester, it becomes clear that a successful catalyst aimed to produce high yields of alcohol in a one-pot reaction should be able to perform the BV reaction in the presence of water, while catalyzing rapidly the hydrolysis of the ester formed in the first oxidation step. Thus, in order to couple the two reactions, i.e., oxidation and hydrolysis, the process was carried out introducing different amounts of water in the reaction media, and using first the Sn-Beta catalyst. The results presented in Table 1 show that the oxidation activity of the Sn-Beta zeolite is practically not affected by the presence of water. However, the rate of hydrolysis of the ester **2a** increases when increasing the water content, reaching selectivities higher than 95% to the methoxyphenol (**3a**). If the hydrolysis should be avoided the reaction can be carried out with a deficit of hydrogen peroxide. Employing only 0.35 eq, the ester **2a** is observed in a relative selectivity of 90% (Table 2, entry 1). Furthermore, under these conditions the hydrogen peroxide is consumed almost completely. This indicates that competitive decom-

Table 2
BV oxidation of aldehyde **1a** with different amounts of hydrogen peroxide (50%) in acetonitrile

Entry	H_2O_2	TON	Conversion **1a**	Conversion H_2O_2	Product distribution		
	(eq.)		(%)	(%)	Ester **2a**	Alcohol **3a**	Other
1	0.35	169	31	88	90	10	0
2	0.45	199	36	80	89	11	0
3	0.80	242	44	57	83	17	0
4	1.0	285	51	51	72	28	0
5	1.2	317	56	46	54	46	0

Reaction conditions: 0.5 g of aldehyde **1a**, 50% aqueous hydrogen peroxide (amount as indicated), 3.0 g of acetonitrile, and 50 mg of catalyst Beta-1 (Sn-Beta) were stirred for 7 h at 353 K.

Table 3
Influence of the solvent on the hydrolysis of the ester to the alcohol

Entry	Water	Solvent	TON	Conversion	Product distribution		
	(mg)			(%)	Ester **2a**	Alcohol **3a**	other
1	–	Acetonitrile	317	56	54	46	0
2	500	Acetonitrile	327	59	4	96	0
3	–	Dioxane	259	46	77	23	0
4	500	Dioxane	106	19	54	46	0
5	–	Ethanol	317	57	1	99	0
6	500	Ethanol	244	44	5	95	0
7	–	DMSO	5	1	46	54	0
8	500	DMSO	5	1	55	45	0

Reaction conditions: 0.5 g of aldehyde **1a**, 0.30 g of 50% aqueous hydrogen peroxide, 3.0 g of solvent, water (when indicated), and 50 mg of catalyst Beta-1 (Sn-Beta) were stirred for 7 h at 353 K.

position of hydrogen peroxide does not occur and the selectivity with respect to the oxidant is excellent.

3.1. Influence of the solvent for the Sn-Beta catalyst

If one takes into account that in the present reaction two molecules with different polarities, i.e., H_2O_2 (aq) and *para*-anisaldehyde have to diffuse through the zeolite pores and adsorb on the catalyst surface, it becomes clear that despite the catalyst properties the polarity of the solvent should also play an important role on the final catalytic behavior. In order to study this, the Baeyer–Villiger rearrangement of *para*-anisaldehyde (**1a**) was carried out in four different solvents: acetonitrile, dioxane, ethanol, and dimethyl sulfoxide (DMSO). The results are summarized in Table 3 and they show that when one goes from the less polar solvent, dioxane, to the more polar acetonitrile and ethanol, the activity of the catalyst increases. Furthermore, the selectivity to products **2a** and **3a** is strongly affected by the nature of the solvent, in such a way that the phenol selectivity increases in the same order as the polarity of the solvent: ethanol > acetonitrile > dioxane. In fact, when using ethanol as solvent, it is possible to obtain phenol **3a** with 99% selectivity (Table 3, entry 5). These findings indicate that the transition-state complex (TSC) which leads to the ester as well as the one which leads to the ester hydrolysis is better stabilized when the solvent polarity is higher, decreasing the free enthalpy of the TSC and enhancing the reaction rate of both processes. On the other hand, when the ester **2a** is the desired product dioxane should be the solvent of choice. Under the best conditions the ester **2a** can be obtained with a 77% selectivity at a conversion of 46% (Table 3, entry 3).

When DMSO was used as solvent, the activity of the catalysts was very low, achieving less than 5% of conversion after 7 h of reaction time (Table 3, entry 7). This result might be attributed to the strong adsorption of the DMSO on the active Sn centers through the oxygen of the sulfoxide group.

The effect of the water concentration was studied with the different solvents and it was found that in the case of the protic solvent ethanol, the water addition decreases the conversion significantly and has a minor effect on the rate of hydrolysis (Table 3, entries 5 and 6), while using ethanol as solvent the hydrolysis was already completed without further water addition. In the case of the polar aprotic solvent dioxane, the catalyst activity is also lowered when increasing water concentration (Table 3, entries 3 and 4). For the product selectivity an increase of hydrolysis was observed and at longer reaction times the product ratio was shifted more and more toward phenol **3a** as it has been described already for acetonitrile.

From these results we can conclude that the selectivity to ester **2a** and phenol **3a** can be modified by using the adequate solvent. In dioxane the ester **2a** is the predominant product whereas in ethanol or aqueous acetonitrile the phenol **3a** is obtained almost exclusively.

3.2. Nature and optimization of the catalytic active sites

We have seen above the influence of solvent and H_2O content on the relative selectivity to ester and alcohol. How-

Table 4
Different Al and Sn contents in Beta catalysts in the Baeyer–Villiger oxidation of *para*-anisaldehyde (**1a**) with hydrogen peroxide (50%) in acetonitrile

Entry	Catalyst			Conversion	Product distribution		
		SnO_2 (wt%)	Si/Al ratio (mol/mol)	(%)	**2a**	**3a**	Other
1	Beta-1	2.0	> 10,000	56	54	46	0
2	Beta-2	2.6	100	74	11	87	2[a]
3	Beta-3	2.4	28	78	5	89	6[a]
4	Beta-4	0.0	> 10,000	3	84	16	0
5	Beta-5	0.0	250	84	17	83	0
6	Beta-6	0.0	100	79 (61)	8 (51)	79 (39)	12 (10)[a]
7	Beta-7	0.0	30	87 (70)	1 (47)	95 (50)	4 (3)[a]
8	Beta-8	0.0	15	83	11	86	3

Reaction conditions: 0.5 g of aldehyde **1a**, 0.30 g of 50% aqueous hydrogen peroxide, 3.0 g of acetonitrile, and 50 mg of a catalyst sample were stirred for 7 h at 353 K. Values in parentheses were obtained after 1 h reaction time.
[a] Mainly anisic acid **4a**.

ever, there is another way to modify the relative rate of the oxidation and hydrolysis reaction, namely by introducing Brønsted acid sites into the Lewis-type Sn-Beta zeolite catalyst. Indeed, the presence of Brønsted acidity in the catalyst should increase the rate of hydrolysis and therefore should increase the yield of alcohol. In order to study this hypothesis a series of zeolites with very close amounts of Sn but with different framework aluminum content were synthesized. If one takes into account that an acidic bridging hydroxyl group should be formed per each framework aluminum, we have prepared catalysts with different ratios of oxidating (Sn) to hydrolysis (H^+) active sites (see Table 4). When these catalysts were tested for the BV reaction of *para*-anisaldehyde, it could be seen that the yield of the alcohol (**3a**) increases when increasing the framework aluminum in the Sn-Beta zeolite. What appears more interesting is that conversion is enhanced when increasing the Brønsted acidity of the zeolite, indicating that the bridging hydroxyls can also be active sites for the BV oxidation of aldehydes. Thus, we have prepared a series of Sn-free Al-Beta zeolites with different framework Si/Al ratios, and they show an excellent catalytic activity. However, it appears that Al-Betas are globally less selective than Sn-Beta since the former produces larger amounts of subproducts, specially anisic acid, indicating that they also catalyze the migration of the H atom besides the migration of the aromatic moiety. Note that this lower selectivity is not an effect of the conversion level, since when similar levels of conversion are compared (Table 4, entries 1, 6, and 7), the amounts of subproducts produced with Sn-Beta are clearly lower.

3.3. Mechanism of the reaction and the effect of the substituent in the aromatic ring

In the study of the Baeyer–Villiger oxidation of cyclic ketones to lactones using the system Sn-beta/H_2O_2 we have shown, by means of ^{18}O-labeled 2-methylcyclohexanone, that the mechanism of the Baeyer–Villiger oxidation with hydrogen peroxide proceeds through a Criegee adduct of the hydrogen peroxide with the ketone substrate [15,16]. In that

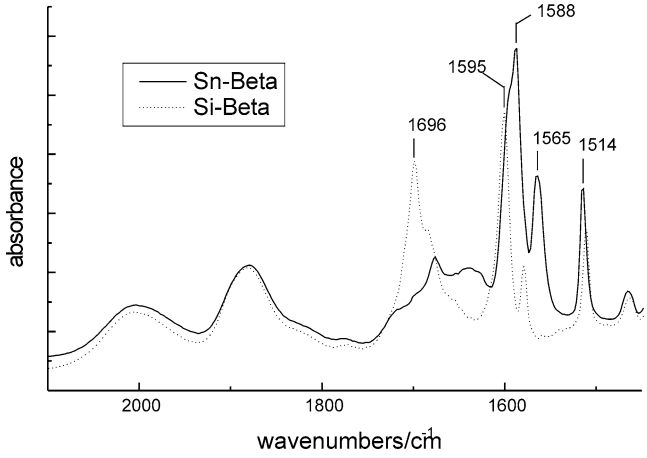


Fig. 2. Adsorption and desorption of *para*-anisbenzaldehyde measured by "in situ" IR spectroscopy. In the case of Sn-Beta (Beta-1) the displayed spectrum was obtained after desorption at 373 K and in the case of Si-Beta (Beta-4) after desorption at 323 K.

case, Sn-Beta does not activate the H_2O_2 but the carbonyl group by coordination with the Lewis-acidic Sn center.

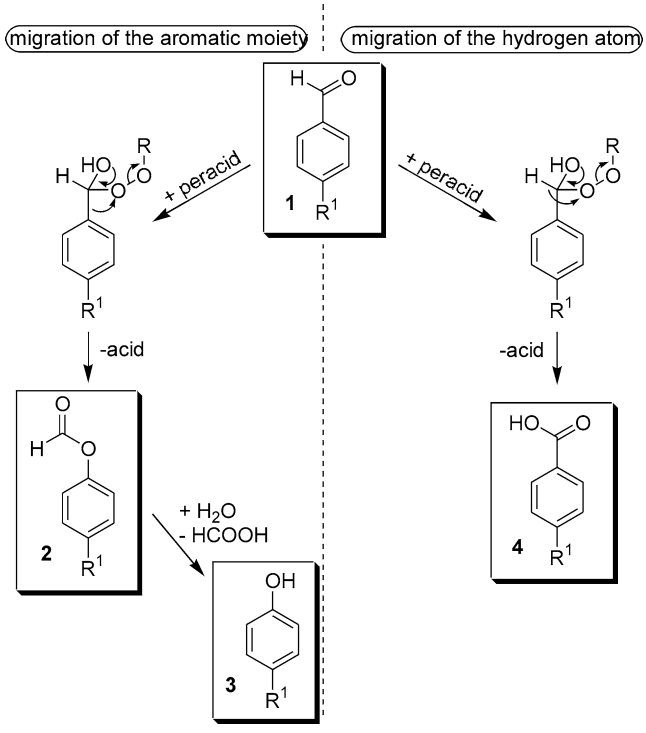
In order to see if the same reaction model applies to the oxidation of aldehydes, we have adsorbed a comparable amount of *para*-anisaldehyde on pure silica Beta (Beta-4) and on Sn-Beta (Beta-1) samples in a vacuum IR cell. It can be seen in Fig. 2 that for Si-Beta, the carbonyl band appears at 1696 cm^{-1} which corresponds to the physically adsorbed *para*-anisaldehyde. When the sample was heated at 373 K the product desorbs and the 1696 cm^{-1} band disappears. In the case of the Sn-Beta catalyst, after heating at 373 K a band at 1588 cm^{-1} remains. This corresponds to adsorbed aldehyde in which the 1696 cm^{-1} band is shifted to 1588 cm^{-1} owing to the interaction of the carbonyl band of the aldehyde with the Sn Lewis acid center. This result indicates that also in the case of aromatic aldehydes an activation of the carbonyl group by the Sn sites occurs that facilitates the nucleophilic attack of the H_2O_2 to the corresponding carbon atom.

If the above is true, the electron donor properties of different substituents in the benzene ring should have an influence on conversion and selectivity. From the results presented

Table 5
Baeyer–Villiger oxidation of benzaldehydes involving different *para* substituents with hydrogen peroxide catalyzed by Sn-Beta

Entry	Substrate		Conversion	Product distribution		
		R	(%)	**2** + **3**	**4**	Other
1	**1a**	OMe	56	> 99	0	0
2	**1b**	OEt	69	> 99	0	0
3	**1c**	OnPr	82	> 99	0	0
4	**1d**	OPh	70	> 99	0	0
5	**1e**	Me	32	72	28	0
6	**1f**	*t*Bu	13	52	43	5
7	**1g**	H	19	0	> 99	0

Reaction conditions: 0.5 g of aldehyde **1**, 0.30 g of 50% aqueous hydrogen peroxide, 3.0 g of acetonitrile, and 50 mg of catalyst Beta-1 (Sn-Beta) were stirred for 7 h at 353 K.



Scheme 2. Baeyer–Villiger reaction of aromatic aldehydes **1**. The aldehyde **1** and the oxidant first form the "Criegee Intermediate," and then migration of the aromatic ring leads to the formate ester **2** which can be hydrolyzed to the phenol **3** (left-hand side). Migration of the hydrogen atom in the Criegee Intermediate yields the corresponding carboxylic acids **4** (right-hand side).

in Table 5 it becomes apparent that conversion decreases when the electron donor capacity of the group in *para* position decreases. A parallel effect is observed for the product selectivity which is shifted more and more from 100% migration of the aromatic moiety for the alkoxy sustituents (cf. Scheme 2, left-hand side) to yield ester **2** and alcohol **3**, to proton migration which yields the acid **4** (Scheme 2, right-hand side). It seems that the migration ability of the aromatic unit is improved by electron-donating substituents in *para* position enhancing the reaction rate and favoring its migration over the alternative hydrogen migration. A similar effect has been found for the BV reaction of mono-substituted benzophenones with peracids [20]. However, it has also been pointed out that not only the migration ability is modified by different aromatic substituents but also the electronic nature of the carbonyl bond and therewith the nucleophilic attack of the hydrogen peroxide onto the carbonyl carbon atom [20]. Indeed, from in situ IR measurements this effect might be confirmed here. Fig. 3 shows the corresponding IR spectra of methylbenzaldehyde **1e** and benzaldehyde **1g**. The carbonyl band for both compounds (physisorbed) can be found at 1705 versus 1696 cm^{-1} observed for physisorbed *para*-methoxybenzaldehyde (cf. Fig. 3). The difference is even more pronounced for the chemisorbed derivatives. Here, the value of ca. 1635 cm^{-1} for aldehydes **1e** and **1g** (Fig. 3) is changed to 1588 cm^{-1} for aldehyde **1a** (Fig. 2). In summary, it can be concluded that electron donating substituents in the *para* position of the benzaldehyde enhance the reaction rate by favoring the nucleophilic attack on the carbonyl group and lowering the activation energy for the migration of the aromatic moiety. Both effects are beneficial for the selectivity toward the ester and alcohol (cf. Scheme 2, left pathway) and, consequently, the ester is the only primary product observed in the case of alkoxy benzaldehydes with a pronounced positive mesomeric effect.

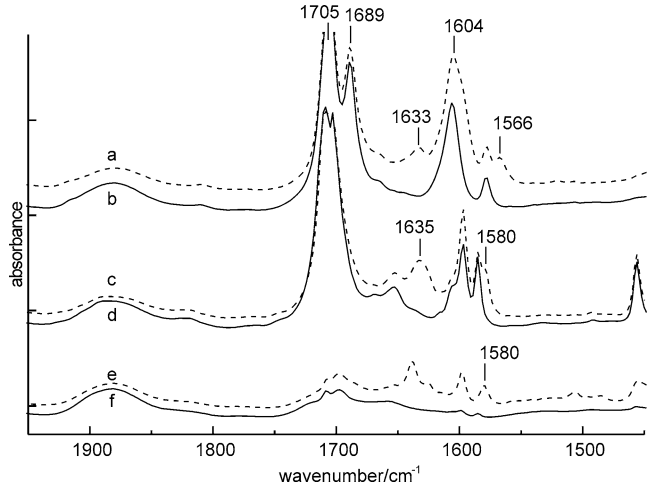
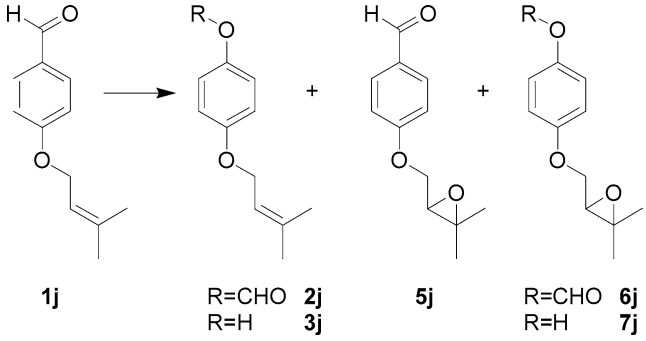


Fig. 3. IR spectra for Beta-1 (spectra a, c, and e) and Beta-4 (spectra b, d, and f) samples after adsorption and desorption of *para*-methylbenzaldehyde (**1e**, spectra a and b) and of benzaldehyde (**1g**, spectra c to f). The desorption temperature was 323 K for spectra a, b, e, and f, and 298 K for spectra c and d.

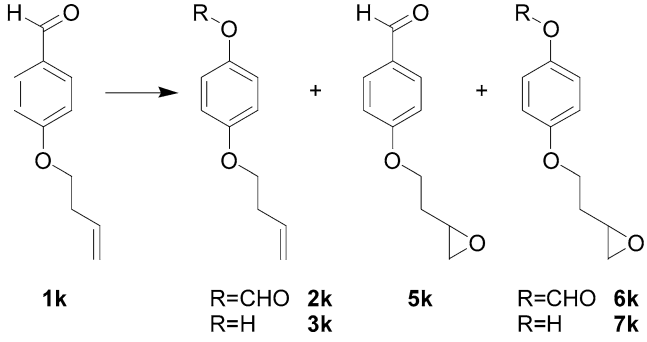
Finally, the influence of the position of a methoxy group in the aromatic ring on the catalyst activity was studied. The highest catalytic activity is found for aldehyde **1a** with the substituent in *para* position (Table 6, entry 1), followed by the *ortho* isomer (Table 6, entry 3). However, when the methoxy group is placed in the *meta* position, a low conversion is achieved, being *meta*-methoxy benzoic acid (**4h**) the main product detected in the reaction mixture. This result is not surprising having in mind that the mesomeric effect of the *meta* substituent cannot influence the electronic nature of the carbonyl bond or of the migrating atom. The lower conversion for the *ortho* aldehyde versus the *para* isomer is

Table 6
Baeyer–Villiger oxidation of *para*, *meta*, and *ortho*-methoxybenzaldehyde with hydrogen peroxide catalyzed by Sn-Beta

Entry	Aldehyde		TON	Conversion	Product distribution		
				(%)	Ester **2** phenol **3**	Acid **4**	Other
1	*para*	**1a**	291	56	> 99	0	0
2	*meta*	**1h**	70	12	0	81	19
3	*ortho*	**1i**	134	46	> 99	0	0



Scheme 3.



Scheme 4.

probably due to steric hindrance of the two neighbored substituents which might render more difficult the formation of the transition state. A similar trend has been observed for the BV oxidation with peracids [20].

3.4. Synthesis of phenols with industrial interest

It has been reported that the phenols 4-(3-methyl-2-butenoxy)-phenol (**3j**, Scheme 3) and 4-(3-butenoxy)-phenol (**3k**, Scheme 4) are intermediates for the production of a thermotropic liquid crystal polymers used in cosmetic compositions for human skin and/or lips [21], and for the synthesis of effective insecticides against houseflies [22], respectively. They might be produced by the BV oxidation of 4-(3-methyl-2-butenoxy)-benzaldehyde (**1j**) and 4-(3-butenoxy)-benzaldehyde (**1k**). However, both starting molecules have in common a *para* substituent bearing a double bond. Thus, the BV oxidation of those molecules will require not only active but also chemoselective oxidants since the epoxidation of the double bond must be avoided.

In Table 7 the results for the BV oxidation of aldehyde **1j** are presented using the Sn-Beta and Al-Beta/H_2O_2 oxidation

Table 7
Chemoselectivities for different oxidation methods in the Baeyer–Villiger oxidation of *para*-(3-methylbut-2-enoxy)-benzaldehyde (**1j**)

Entry	Oxidation system	Conversion	Product distribution			
		(%)	**2j** + **3j**	**5j**	**6j** + **7j**	Other
1	H_2O_2, Beta-1	61	85[a]	0	0	15[b]
2	H_2O_2, Beta-7	0	0	0	0	0
3	H_2O_2, MTO[c]	15	0	75	4	21
4	H_2O_2, MTO[d]	66	0	62	6	32
5	mCPBA[e]	20	28	12	29	31

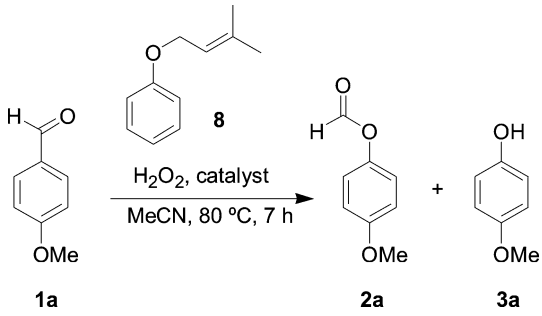
[a] 1:4 ratio of ester **2j** to alcohol **3j**. [b] Unidentified higher oxidation products excluding epoxide **5j**. [c] In acetonitrile. [d] Reaction conditions similar as in Ref. [23]; a etheric solution of hydrogen peroxide is used. [e] Only 0.3 eq of the oxidant was employed.

Table 8
Chemoselectivities for different oxidation methods in the Baeyer–Villiger oxidation of *para*-(3-butenoxy)-benzaldehyde (**1k**)

Entry	Oxidation system	Conversion	Product distribution			
		(%)	**2k** + **3k**	**5k**	**6k** + **7k**	Other
1	H_2O_2, Beta-1	41	> 99[a]	0	0	0
2	H_2O_2, Beta-7	0	0	0	0	0
3	mCPBA[b]	22	> 99	0	0	0

[a] 2:3 ratio of ester **2k** and alcohol **3k**. [b] Only 0.4 eq of oxidant was employed.

systems and they are compared with those obtained when methyltrioxorhenium/H_2O_2 and *meta*-chloroperbenzoic acid are used as oxidants. It can be seen that mCPBA gives a mixture of all possible oxidation products from BV oxidation and epoxidation (Table 7, entry 5 and Scheme 3). The MTO/H_2O_2 oxidant shows a high epoxidation activity but less BV activity. Consequently, the BV products **2j** and **3j** are not observed and, if formed, they are oxidized further to the corresponding epoxidized BV products **6j** and **7j** which are the by-products for the epoxide **5j** (Table 7, entries 3 and 4). Sn-Beta (catalyst Beta-1) is active and selective for the BV oxidation yielding mainly compounds **2j** and **3j** (Table 7, entry 1), whereas, surprisingly, Al-Beta (Beta-7) was not active at all (Table 7, entry 2). When aldehyde **1k** was used as substrate (Table 8 and Scheme 4) we found similar results using both zeolites as catalysts. Thus, whereas Sn-Beta yielded exclusively the ester **2k** and the phenol **3k** (Table 8, entry 1), the Al-Beta was an inactive catalyst (Table 8, entry 2). The peracid yields exclusively compounds **2k** and **3k** in this case probably due to the low activation



Scheme 5.

Table 9
Oxidation of *para*-anisaldehyde in the presence and absence of the potential poison molecule **8**

Entry	Catalyst	Alkene **8** (eq)[a]	Conversion (%)	**2a**	**3a**
1	Beta-1[b]	0	56	54	46
2	Beta-1	1.0	19	13	87
3	Beta-7[c]	0	87	1	95
4	Beta-7	1.0	2	79	21

[a] With respect to anisaldehyde. [b] From Table 1. [c] From Table 4.

of the monosubstituted double bond toward the epoxidation (Table 8, entry 3).

The lack of activity of Al-Beta zeolite could be attributed to a preferential interaction of the substrate with the Brønsted acid sites through the double bond instead of through the carbonyl group. Then, deactivation may derive from two different effects:

(i) formal replacement of catalytically active protons by fairly stable unreactive carbocations and therewith neutralizing the active sites for the BV oxidation, and
(ii) blocking of the pores by these strongly adsorbed bulky reaction intermediates [24,25].

In order to check the hypothesis presented above, we did an additional experiment where the BV oxidation of the *para*-anisaldehyde was carried out in the presence of 3-methyl-2-butenoxybenzene (**8**) using Beta-1 and Beta-7 as catalysts (Scheme 5). It can be seen that for Sn-Beta the conversion decreases in the presence of this potential poison molecule (Table 9, entries 1 and 2), probably due to competitive adsorption and diffusion within the catalyst channels. However, Beta-7 suffers by far stronger deactivation with only 2% of conversion of aldehyde **1a** after 7 h reaction time (Table 9, entries 3 and 4). These results allow us to conclude that deactivation observed for the Al-Beta zeolite is due to the interaction of the Brønsted acid sites with the double bond of the substrate. In contrast for the Lewis-acidic Sn sites, a significant deactivation in the presence of double bond has not been detected.

Table 10
Recycling of the Sn-Beta catalyst without treatment in the Baeyer–Villiger oxidation of *para*-anisaldehyde (**1a**) with hydrogen peroxide (50%)

Entry	Special treatment	Cycle	TON	Conversion (%)
1		1	282	51
2		2	199	36
3		3	237	43
4		4	222	38
5	Recalcination	4/1	282	51
6		1	277	50
7	Extraction	1/1	207	37

The selectivity toward ester **2a** and alcohol **3a** was always > 98%.

3.5. Deactivation and regeneration of Sn-Beta

In order to study the catalyst deactivation during the BV oxidation, we have carried out four reaction cycles with *para*-anisaldehyde using Beta-1 as catalyst and acetonitrile as solvent. At the end of each reaction the catalyst sample was filtered out and submitted to the next run after activation at 473 K in vacuum. In Table 10 the results for Sn-Beta (Beta-1) obtained after four cycles are presented showing a decrease in activity from the first to the second cycle (Table 10, entry 2), with no further decrease in the subsequent cycles. The loss of activity might be mainly due to the block of the active sites and/or channels by organic material. In fact, when, the used catalyst was soxhlet-extracted with ethanol or acetone as solvent, aldehyde **1a** and ester **2a** could be detected in the extract. However, when the soxhlet-extracted catalyst was reused, the activity was not improved (cf. Table 10, entries 2 and 7). The TG analysis of this extracted zeolite sample showed that 4 wt% of organic material still remained on the catalyst.

IR spectroscopy on the catalyst after the reaction without any treatment confirmed the presence of physisorbed aldehyde **1a**. A temperature treatment of 473 K in vacuum was able to remove the aldehyde completely and a spectrum of a single compound (sharp bands) was observed (spectrum not shown). Three characteristic bands can be attributed very clearly the to ester **2a**, namely 1727 cm^{-1} for the carbonyl group of a formate ester, and 1602 and 1508 cm^{-1} for the aromatic moiety. All these data indicate that there is still some ester **2a** adsorbed in a used catalyst sample which was not removed by activation at 473 K. However, when the catalyst, used in four cycles, was regenerated by calcination at 853 K for 3 h in air, the initial activity was fully recovered (cf. Table 10, entries 1 and 5). When the same reaction protocol was carried out under reaction conditions that favor the hydrolysis of the ester and the production of alcohol, the catalytic performance of the catalyst was very similar.

4. Conclusions

The heterogeneous oxidation systems Sn-Beta/H_2O_2 and Al-Beta/H_2O_2 are both active for the Baeyer–Villiger oxida-

tion of aromatic aldehydes. With alkoxy substituents in *ortho* and especially in *para* position the corresponding formate ester is the primary reaction product with excellent selectivity. The highest selectivity toward the ester is obtained with the Sn-Beta catalyst in dioxane as solvent. High selectivities of the corresponding phenol can be obtained by employing ethanol or aqueous acetonitrile as solvent with Sn-Beta. Al-Beta is more efficient as catalyst for both Baeyer–Villiger oxidation and ester hydrolysis and, therefore, achieves high yields for the corresponding alcohol. However, this is a less selective catalyst than Sn-Beta zeolite. It must be pointed out that Sn-Beta is a chemoselective catalyst when the aldehyde reactant contains olefinic groups in an alkyl chain. With these reactants the Al-zeolite gives no activity. Other classical BV oxidants such as peracids also yield the epoxidation products. Thus Sn-Beta catalysts open a new entry to aromatic phenols with unsaturated alkyl substituents which are interesting intermediates in the chemical industry. The mechanism for the Baeyer–Villiger oxidation of aromatic aldehydes catalyzed by Sn-Beta is supposed to be similar to the one for cyclic ketones and start with the activation of the carbonyl bond by coordination to the Lewis acidic center followed by a nucleophilic attack of the hydrogen peroxide onto the more electrophilic carbonyl carbon atom.

Acknowledgments

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References

[1] T. Saito, T. Hirayama, S. Sakagushi, JP 08151343, 1996.
[2] T. Sato, H. Matsumoto, T. Kakegawa, Y. Niino, JP 05301836, 1993.
[3] Y. Nihro, H. Furukawa, S. Sogawa, T.C. Wang, H. Miyataka, H. Matsumoto, T. Miki, T. Satoh, Chem. Pharm. Bull. 42 (1994) 576–579.
[4] K. Schwabe, J. Redslob, D. Breitfeld, R. Zeisig, B. Tschiersch, W. Wohlrab, K.D. Wozniak, C. Bayer, C. Nowak et al., DD 287482, 1991.
[5] P.A. Riley, C.J. Cooksey, C.I. Johnson, E.J. Land, A.M. Latter, C.A. Ramsden, Eur. J. Cancer 33 (1997) 135–143.
[6] U. Wellnitz, S. Potsch, C. Garbe, G. Lassmann, Melanoma Res. 7 (1997) 288–298.
[7] G. Laßmann, S. Pötsch, DE 4344645, 1995.
[8] M.T. Caproiu, A.A. Banciu, E. Olteanu, RO 105090, 1994.
[9] G.R. Krow, Org. React. 43 (1993) 251–798.
[10] I.M. Godfrey, M.V. Sargent, J.A. Elix, J. Chem. Soc. Perkin Trans. 1 (1974) 1353–1354.
[11] N. Anoune, H. Hannachi, P. Lantéri, R. Longeray, C. Arnaud, J. Chem. Ed. 75 (1998) 1290–1293.
[12] L. Syper, Synthesis (1989) 167–172.
[13] M. Matsumoto, H. Kobayashi, Y. Hotta, J. Org. Chem. 49 (1984) 4740–4741.
[14] R.H. Dodd, M. Le Hyaric, Synthesis (1993) 295–297.
[15] A. Corma, L.T. Nemeth, M. Renz, S. Valencia, Nature 412 (2001) 423–425.
[16] M. Renz, T. Blasco, A. Corma, V. Fornés, R. Jensen, L. Nemeth, Chem. Eur. J. 8 (2002) 4708–4717.
[17] A. Corma, M.T. Navarro, L. Nemeth, M. Renz, Chem. Commun. (2001) 2190–2191.
[18] S. Valencia, A. Corma, UOP LCC, US 5968473A, 1999.
[19] A. Mann, C. Muller, E. Tyrrell, J. Chem. Soc. Perkin Trans. 1 (1998) 1427–1438.
[20] M. Renz, B. Meunier, Eur. J. Org. Chem. (1999) 737–750.
[21] F. Tournilhac, WO patent 0238112, 2001.
[22] C.A. Henrick, EP patent 169169, 1985.
[23] A.M.F. Phillips, C. Romão, Eur. J. Org. Chem. (1999) 1767–1770.
[24] A. Corma, H. García, J. Chem. Soc. Dalton Trans. 9 (2000) 1381–1394.
[25] J.F. Haw, Phys. Chem. Chem. Phys. 4 (2002) 5431–5441.