Zeolite Catalysts for Phenol Benzoylation with Benzoic Acid: Exploring the Synthesis of Hydroxybenzophenones

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Abstract: In this paper, we report on the reaction of phenol benzoylation with benzoic acid, which was carried out in the absence of solvent. The aim of this reaction is the synthesis of hydroxybenzophenones, which are important intermediates for the chemical industry. H-beta zeolites offered superior performance compared to H-Y, with a remarkably high conversion of phenol and high yields to the desired compounds, when using a stoichiometric amount of benzoic acid. It was found that the reaction mechanism did not include the intramolecular Fries rearrangement of the primary product phenyl benzoate, but indeed, the bimolecular reaction between phenyl benzoate and phenol mainly contributed to the formation of hydroxybenzophenones. The product distribution was greatly affected by the presence of Lewis-type acid sites in H-beta; it was suggested that the interaction between the aromatic ring and the electrophilic Al$^{3+}$ species led to the preferred formation of o-hydroxybenzophenone, because of the decreased charge density on the C atom at the para position of the phenolic ring. H-Y zeolites were efficient than H-beta in phenyl benzoate transformation into hydroxybenzophenones.

Keywords: phenol; benzoic acid; hydroxybenzophenone; H-beta; benzoylation; acylation
1. Introduction

The acylation of phenolic compounds is an important class of reactions with several applications in the chemical industry [1,2]. In fact, aromatic hydroxy ketones are intermediates for the synthesis of various pharmaceuticals and fragrances. $p$-Hydroxyacetophenone and $o$-hydroxyacetophenone are used for the synthesis of paracetamol and aspirin, respectively; the ortho isomer is also an intermediate for the synthesis of 4-hydroxycoumarin and flavanones. Furthermore, the acylation of resorcinol is an important process for the synthesis of a precursor for the UV-light absorbent for polymers, 4-$o$-octyl-$o$-hydroxybenzophenone [3].

In general, these reactions are catalyzed by homogeneous Friedel-Crafts Lewis-type catalysts; however, due to the environmental problems associated with the use of these compounds, alternative heterogeneous systems have been sought and, in some cases, successfully implemented in industrial uses. Furthermore, zeolites have been widely studied as catalysts for the acylation of both aromatic hydrocarbons and phenolics; several reports describe the reaction of these substrates, mainly in the liquid phase, but also in the gas phase, with different acylating agents, such as acyl halides (typically benzoyl chloride and acetyl chloride), anhydrides and even aliphatic and aromatic carboxylic acids, which are typically considered poorly reactive and, thus, react preferably with activated substrates [1,4–39].

A summary of acylations where the catalyst is made up of a zeolite is shown in Table 1. Amongst the various zeolites tested, H-beta typically offers a superior performance in terms of reactant conversion and selectivity to the desired product; this was suggested to be due to its pore structure. In some cases, however, H-Y also showed excellent performances.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Acylating Reagent</th>
<th>Desired Product</th>
<th>Catalyst</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexene</td>
<td>Acetic anhydride, acetyl chloride</td>
<td>Acetylcyclohexenes</td>
<td>H-Y, H-beta, H-mordenite</td>
<td>[33]</td>
</tr>
<tr>
<td>Benzene</td>
<td>Benzoyl chloride</td>
<td>Benzophenone</td>
<td>Ga, In-H-beta</td>
<td>[26]</td>
</tr>
<tr>
<td>Toluene</td>
<td>Phthalic acid</td>
<td>2-methylanthraquinone</td>
<td>H-Y, H-beta, H-mordenite</td>
<td>[39]</td>
</tr>
<tr>
<td>Toluene</td>
<td>Benzoyl chloride</td>
<td>4-methylbenzophenone</td>
<td>H-beta</td>
<td>[4]</td>
</tr>
<tr>
<td>Toluene</td>
<td>Acetic anhydride</td>
<td>4-methylacetophenone</td>
<td>H-beta (nano)</td>
<td>[8]</td>
</tr>
<tr>
<td>$o$-Xylene</td>
<td>Benzoyl chloride</td>
<td>3,4-dimethylbenzophenone</td>
<td>H-beta</td>
<td>[6]</td>
</tr>
<tr>
<td>$m$-Xylene</td>
<td>Benzoyl chloride, benzoic anhydride</td>
<td>2,4-dimethylbenzophenone</td>
<td>H-Y</td>
<td>[40]</td>
</tr>
<tr>
<td>Naphthalene</td>
<td>Benzoyl chloride</td>
<td>2-benzoylnaphthalene</td>
<td>H-beta</td>
<td>[5]</td>
</tr>
<tr>
<td>2-Methoxynaphthalene</td>
<td>Acetic anhydride</td>
<td>2-acetyl-6-methoxynaphthalene</td>
<td>H-beta, H-Y, ITQ-7</td>
<td>[7,13,22,25,41]</td>
</tr>
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<td>Biphenyl</td>
<td>Acetic anhydride</td>
<td>4-acetylbiphenyl</td>
<td>H-Y, H-beta</td>
<td>[12]</td>
</tr>
<tr>
<td>Biphenyl</td>
<td>Benzoyl chloride</td>
<td>4-phenylbenzophenone</td>
<td>H-beta</td>
<td>[20]</td>
</tr>
<tr>
<td>Chlorobenzene</td>
<td>4-chlorobenzoic chloride</td>
<td>4,4′-dichlorobenzophenone</td>
<td>H-beta</td>
<td>[14]</td>
</tr>
<tr>
<td>Phenol</td>
<td>Propionyl chloride</td>
<td>4- and 2-hydroxypropionophenone</td>
<td>H-beta</td>
<td>[10]</td>
</tr>
<tr>
<td>Phenol (gas-phase)</td>
<td>Acetic acid</td>
<td>$p$- and $o$-hydroxyacetophenone</td>
<td>Zn-exchanged NaY or ZSM-5</td>
<td>[42]</td>
</tr>
<tr>
<td>Phenol</td>
<td>Benzoic anhydride</td>
<td>$p$- and $o$-hydroxybenzophenone</td>
<td>H-beta</td>
<td>[19]</td>
</tr>
<tr>
<td>Substrate</td>
<td>Acylating Reagent</td>
<td>Desired Product</td>
<td>Catalyst</td>
<td>Ref</td>
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<tr>
<td>Phenol</td>
<td>Acetic anhydride</td>
<td>p- and o-hydroxyacetophenone</td>
<td>H-ZSM5 (Cu-, Co-doped)</td>
<td>[37]</td>
</tr>
<tr>
<td>Phenol</td>
<td>Acetic acid</td>
<td>p- and o-hydroxyacetophenone</td>
<td>HZSM-5, H-Y</td>
<td>[38,43]</td>
</tr>
<tr>
<td>Phenol</td>
<td>Phenylacetate</td>
<td>p- and o-hydroxyacetophenone</td>
<td>H-beta</td>
<td>[44]</td>
</tr>
<tr>
<td>p-Cresol</td>
<td>Acetic acid, propionic acid, butyric acid, etc.</td>
<td>Various o-hydroxy ketones</td>
<td>H-beta</td>
<td>[45]</td>
</tr>
<tr>
<td>Anisole</td>
<td>Octanoic acid</td>
<td>p-octanoyl anisole</td>
<td>H-beta</td>
<td>[24]</td>
</tr>
<tr>
<td>Anisole</td>
<td>Hexanoic, octanoic, decanoic acids</td>
<td>4-methoxyphenylalkylketone</td>
<td>H-beta, H-Y, H-mordenite</td>
<td>[29]</td>
</tr>
<tr>
<td>Anisole</td>
<td>Acetic anhydride</td>
<td>p- and o-methoxyacetophenone</td>
<td>H- beta, H-Y</td>
<td>[32,36]</td>
</tr>
<tr>
<td>Guaiacol</td>
<td>Acetic anhydride</td>
<td>2-methoxyphenyl acetate</td>
<td>H-Ferrierite</td>
<td>[16]</td>
</tr>
<tr>
<td>Veratrole</td>
<td>Propionyl chloride</td>
<td>3,4-dimethoxypropiophenone</td>
<td>H-beta</td>
<td>[17]</td>
</tr>
<tr>
<td>Dimethoxybenzenes</td>
<td>Various acyl chlorides</td>
<td>Various</td>
<td>H-Y</td>
<td>[18]</td>
</tr>
<tr>
<td>Veratrole</td>
<td>Acetic anhydride</td>
<td>3-4-dimethoxyacetophenone</td>
<td>H-Y, H-beta</td>
<td>[9,21]</td>
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<tr>
<td>Phenylacetate</td>
<td>Fries rearrangement</td>
<td>p- and o-hydroxyacetophenone</td>
<td>H-beta</td>
<td>[23,27,46]</td>
</tr>
<tr>
<td>Phenylacetate (gas-phase)</td>
<td>Fries rearrangement</td>
<td>p- and o-hydroxyacetophenone</td>
<td>H_,PO/ZSM-5</td>
<td>[28]</td>
</tr>
<tr>
<td>Phenylacetate</td>
<td>Fries rearrangement</td>
<td>p- and o-hydroxyacetophenone</td>
<td>H-beta, H-Y, H-ZSM5</td>
<td>[34]</td>
</tr>
<tr>
<td>Phenylacetate, phenyl benzoate</td>
<td>Fries rearrangement</td>
<td>p- and o-hydroxyacetophenone</td>
<td>H-ZSM5, H-ZSM12</td>
<td>[35]</td>
</tr>
</tbody>
</table>

Other non-zeolitic, but heterogeneous catalysts have also been used, such as: (i) montmorillonites of the K series for the acetylation of various aliphatic and aromatic substrates [47,48] and of aliphatic and aromatic alcohols [49], for the acylation of resorcinol with phenylacetic chloride [50] and after an exchange with various metals for the reaction between aromatic aldehydes and acetic anhydride to produce the corresponding 1,1-diacetates [51]; (ii) silica-supported phosphotungstic acid for the acylation of aromatic hydrocarbons with acrylic and crotonic acid [52,53], for the Fries rearrangement of phenyl benzoate [54] and for the acylation of anisole with acetic anhydride [55,56]; (iii) clay-supported Cs-phosphotungstic acid for the benzylation of anisole with benzoyl chloride [57], for the benzylation of p-xylene [58,59] and of phenol with benzoic acid (BA) to obtain p-hydroxybenzophenone (HBP) [60]; (iv) giant P/W heteropolyacids for the acetylation of phenol with acetic anhydride [61] (the reactivity of heteropolyacids for Friedel-Crafts acylation was reviewed by Kozhevnikov [62]), and other P/W polyoxometalates for the acetylation of alcohols and phenols [61]; (v) NaGa-Mg hydrotalcite for the benzylation of toluene with benzoyl chloride [63,64]; (vi) EPZG® for the acylation of 1-methoxynaphthalene and anisole with various acyl chlorides and anhydrides [65]; (vii) sulfated zirconia, even promoted with other metal oxides or supported over MCM-41, for the benzylation of anisole with benzoxic anhydride [66–70] or benzoyl chloride [71], for the acylation of phenol, anisole and chlorobenzene with acetic anhydride or benzoic anhydride [72–74], for the acylation of veratrole with acetic anhydride [75] and for the Fries rearrangement of 4-methylphenylbenzoate [76]; (viii) borate zirconia for the benzylation of anisole with benzoyl chloride [77]; (ix) Zr hydroxide functionalized with trifluoromethanesulfonic acid for the benzylation of biphenyl [78]; (x) Sn-doped sulfated zirconia for the benzylation of anisole with benzoyl chloride [79]; (xi) triflic acid-functionalized Zr-TMS
(zirconium oxide with a mesostructured framework; TMS, transition metal oxide mesoporous molecular sieves) for the benzylation of biphenyl [80], of diphenyl ether to 4-phenoxybenzophenone [81] and of toluene to 4,4'-dimethylbenzophenone [82]; (xii) Fe-Zr phosphate for the benzylation of different arenes [83]; (xiii) mesoporous UDCaT-5 (a sulphated tetragonal zirconia-based catalyst) for the acylation of anisole with propionic anhydride [84]; (xiv) KF/alumina for the benzylation of phenolics with benzoyl chloride [85]; (xv) polystyrene-supported GaCl₃ for the benzylation of phenols with benzoic anhydride [86]; (xvi) Fe₃O₄ nanoparticles for the benzylation of phenols with aryl aldehydes to obtain the substituted o-HBPs (xanthones) [87]; (xvii) ZnO for the o-benzylation of alcohols (including phenol) with benzoyl chloride [88,89] and ZnAl₂O₄/SiO₂ composites for the acetylation of alcohols and phenols with acetic anhydride [90]; (xviii) mesoporous Al-KIT-6 (a cubic mesoporous silica with Al incorporated) for the gas-phase acylation of phenol to phenyl acetate with acetic acid [91]; (xix) Al-MCM-41 for the acylation of phenol with acetic acid in the gas-phase [31]; (xx) yttria-zirconia for the acylation of alcohols, thiols and amines with carboxylic acids [92]; (xxi) nafion-in-silica composite for the Fries rearrangement of phenyl acetate [34] and for anisole acylation with acetic anhydride (also with expanded CO₂ as the solvent) [55]; (xxii) WO₃/ZrO₂ for the acylation of veratrole with acetic anhydride and of anisole with benzoic anhydride [93]; and (xxiii) Ni/SiO₂ for the acetylation of phenol, naphthol and other alcohols [94].

In regards to the synthesis of p- and o-HBP (or other substituted benzophenones) or benzyl benzoates via c- or o-benzylation, respectively, papers in the literature describe the use of benzoyl chloride or benzyl trichloride also with various homogeneous catalysts: AlCl₃ for phenol (and phenol derivatives containing 2,2,6,6,-tetramethylpiperidine) [95], Cu(OTf)₂ and Sn(OTf)₂ for anisole and veratrole [96,97], Bi(III) salts for phenol [98] and Hf(OTf)₄ for phenol [99], even with carboxylic acids [100].

As shown in Table 1, there are no papers in the literature describing the use of zeolites for the benzylation of phenol; there is only one paper reporting on phenol benzylation with benzoic anhydride catalyzed by the H-beta zeolite [19] and one paper reporting about the benzylation of phenol with BA using polyoxometalate catalyst [60]. In this latter case, Yadav et al. [60] reported that the first step of the reaction, catalyzed by Cs₂.5H₀.5PW₁₂O₄₀ supported over K-10 clay, is the esterification, which is followed by Fries rearrangement towards hydroxybenzophenones (HBPs). The best selectivity to p-HBP was 32.5% at 70% BA conversion, with a phenol/BA ratio of 7/1. In the paper of Chaube et al. [19], H-beta turned out to be the more active zeolite for the production of HBPs. The selectivity to p-HBP was found to increase with the increase of the strength of acid sites; HBPs formed by both Fries rearrangement and acylation of phenol by phenyl benzoate.

Here, we report on a study aimed at finding zeolitic catalysts and conditions for the liquid-phase benzylation of phenol with BA; the reaction was carried out in the absence of any solvent. Typically, the aim of this reaction is the production of HBPs, which are intermediates for dyes, pharmaceuticals and fragrances. In the current industrial production of HBPs, benzotrichlorides are produced first; they are then reacted with benzene in the presence of AlCl₃, and afterwards, the adduct is hydrolysed into p-HBP. The direct reaction between phenol and BA is also carried out, using BF₃ as a Lewis-type catalyst [19].
2. Results and Discussion

2.1. Characterization of H-Beta Zeolites

Table 2 summarizes the main characteristics of the four H-beta zeolites used: the Si/Al ratio (as stated by the supplier), the overall amount of ammonia desorbed (as determined by NH3-Thermal-Programmed Desorption TPD), and main morphological features. As can be seen, the number of acid sites was not exactly in line with that expected based on the Si/Al ratio; in fact, sample HB-75 had a smaller number of acid sites than HB-150, while the opposite would normally be expected. This seems to be attributable to an overestimation of the number of acid sites in HB-150.

Table 2. Main characteristics of the H-beta (HB) and H-Y (HY) zeolites used as catalysts for phenol benzoylation.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Si/Al, Atomic Ratio</th>
<th>Overall Amount of NH3 Desorbed (mmole NH3/g)</th>
<th>Micropore Volume and Area (cm³/g, m²/g)</th>
<th>Mesopore Volume (cm³/g)</th>
<th>Total Pore Volume (cm³/g)</th>
<th>Total Surface Area (m²/g)</th>
<th>Crystallite Size (nm; from XRD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB-13</td>
<td>13</td>
<td>0.39</td>
<td>0.13, 384</td>
<td>0.55</td>
<td>0.70</td>
<td>575</td>
<td>18</td>
</tr>
<tr>
<td>HB-38</td>
<td>38</td>
<td>0.24</td>
<td>0.15, 421</td>
<td>0.94</td>
<td>1.10</td>
<td>636</td>
<td>16</td>
</tr>
<tr>
<td>HB-75</td>
<td>75</td>
<td>0.11</td>
<td>0.15, 429</td>
<td>0.99</td>
<td>1.16</td>
<td>645</td>
<td>16</td>
</tr>
<tr>
<td>HB-150</td>
<td>150</td>
<td>0.17</td>
<td>0.16, 458</td>
<td>0.17</td>
<td>0.38</td>
<td>641</td>
<td>27</td>
</tr>
<tr>
<td>HY-3</td>
<td>3</td>
<td>1.0 *</td>
<td>Nd</td>
<td>Nd</td>
<td>Nd</td>
<td>584</td>
<td>Nd</td>
</tr>
<tr>
<td>HY-7</td>
<td>7.5</td>
<td>0.1 *</td>
<td>Nd</td>
<td>Nd</td>
<td>Nd</td>
<td>550 *</td>
<td>Nd</td>
</tr>
<tr>
<td>HY-100</td>
<td>100</td>
<td>&lt;0.1 *</td>
<td>Nd</td>
<td>Nd</td>
<td>Nd</td>
<td>814</td>
<td>Nd</td>
</tr>
</tbody>
</table>

Nd: not determined; * as from the TOSOH website.

In regard to the strength of these sites, Figure 1 plots the relative concentration of the Lewis and Brønsted sites, as determined by means of FTIR spectra after pyridine adsorption, taking as reference bands those falling at 1455 and 1545 cm⁻¹, respectively, and using the formula reported in the literature [101]. As can be seen, the sample with the greater Al content showed the higher fraction of strong Lewis sites, which is an expected result based on the fact that the latter is attributable to extra-framework Al species. The strength and relative amount of these Lewis sites decreased when the Si/Al ratio was increased. Conversely, the zeolite with the stronger Bronsted sites was sample H-beta (HB)-150.

We also determined the degree of hydrophilicity of samples by means of H₂O-TPD; Figure 2 shows that, as expected, the increased Si/Al ratio led to samples with a lower affinity for water; however, the molar ratio between adsorbed H₂O molecules and Al atoms increased, suggesting that a higher number of water molecules interacted with more isolated Al sites.
**Figure 1.** Relative concentration of Lewis (♦) and Brønsted (■) sites based on the pyridine desorption temperature, as determined by the intensity of the band associated with the pyridine adsorbed over the two types of sites. Samples: HB-13 (A), HB-38 (B), HB-75 (C) and HB-150 (D).

**Figure 2.** Ratio between amount of H$_2$O adsorbed and catalyst weight (♦) or the number of Al moles (▲), based on the Si/Al atomic ratio. Samples: H-beta zeolites.
2.2. Reactivity of H-Beta Zeolites

Figure 3 plots phenol conversion based on reaction time and product selectivity based on phenol conversion for the four H-beta zeolites studied. There was no obvious relationship between the Al content in zeolites and the catalyst activity. Indeed, comparing phenol conversion at short reaction times, it was shown to increase when the Silica-to-Alumina Ratio SAR ratio decreased from 150 to 38, but then, a further increase in Al content (in sample HB-13) led to its decrease; thus, the most active sample was HB-38. This may mean that the activity was not only related to the number of active acid sites, but also to their strength. It is also important to note that, as reported in the literature, during the liquid-phase acylation of aromatics, the accumulation of heavy compounds may cause catalyst deactivation and a strong inhibition of reactant conversion [27,32,44]. Under our reaction conditions, however, the data shown in Figure 2 seem to rule out important deactivation phenomena; indeed, significant coking phenomena also could be ruled out, because spent catalysts did not appear as being covered by carbonaceous residua. However, HB-13 exhibited a slower rate of conversion increase during time; this might be due to a partial deactivation of Lewis sites (see below for the discussion on the role of acid sites); in fact, HB-13 was the sample showing the greater strength for Lewis acid sites.

Products were phenyl benzoate (PB), o- and p-hydroxybenzophenone (HBP) and o- and p-benzoylphenyl benzoate (BPB); the latter formed with selectivity no higher than 10% and were clearly more prominent with samples having the greatest SAR ratio; in fact, with HB-13, the formation of these compounds was negligible, despite the significant selectivity to HBP, which is a precursor for BPB formation.

With all catalysts, PB was clearly the only primary product, since its selectivity extrapolated at low conversion was 100%. The formation of HBP occurred by consecutive transformations of the ester; it is also interesting to note that the molar ratio between the two HBP isomers (also shown in Figure 3) was very different depending on the sample characteristics. The formation of the para isomer was more facilitated with the catalyst that had the highest Al content (HB-150), with a $p$/o-HBP selectivity ratio much greater than one, while it was less facilitated over the sample with the lowest Al content (HB-13), with a selectivity ratio much lower than one. Furthermore, in all samples, with the exception of HB-13, the para/ortho ratio increased with the increase in phenol conversion, up to a maximum value shown at 20%–40% phenol conversion, after which it decreased; lastly, all samples reached a $p$/o-HBP selectivity ratio close to one.

These trends may have two different interpretations. The first is that two different mechanisms take place for PB transformation into HBPs:

(a) An intramolecular Fries rearrangement of PB, which does not involve phenol, and leads preferentially to the formation of $o$-HBP. The greatest contribution of this reaction is registered with samples having the highest Al content, leading to a $p$/o-HBP selectivity ratio lower than one with HB-13.

(b) An intermolecular reaction between PB and phenol, which leads to both of the two HBP isomers. The greatest contribution of this reaction is registered with samples having the lowest Al content, leading to a $p$/o-HBP selectivity ratio greater than one with HB-150 and HB-75.
An important role in the reaction might be played by the different zeolite properties; with Al-rich zeolites, those showing a greater affinity for more polar molecules (Figure 2), it may be expected that the phenol/BA molar ratio inside pores is greater than with Al-poor zeolites. This might be the reason for the effects shown, i.e.,: (i) a maximum value for the \( p/o \)-HBP selectivity ratio obtained at about
30%–40% phenol conversion; and (ii) a different trend in the selectivity ratio shown by samples, both effects being attributable to a different concentration of the two reactants inside pores and, thus, to a change in the relative contribution of intra- and inter-molecular reactions.

An alternative hypothesis is that the formation of HBP occurs only by means of the bimolecular mechanism between PB and phenol. In this case, the different acidity of zeolites might be the reason for the different $p/o$-HBP selectivity ratio shown. In particular, the stronger Lewis-type acidity shown by the H-beta with higher Al content might be responsible for an enhanced interaction with the phenol aromatic ring, which in turn might entail a lower delocalization of the negative charge over the ring itself; thus, the regio-selectivity of the reaction might be strongly affected by the decreased contribution of the mesomeric effect. Therefore, with catalysts showing the strongest Lewis-type acid sites, the ring-acylation at the ortho position might be more probable over the acylation at the para position, due to the prevailing contribution of the inductive effect, which exerts its effect on the ortho position only.

The trend observed for the $p/o$-HBP selectivity ratio based on phenol conversion, with a maximum value registered at about 30%–40% conversion, may be due to the overlapping of two opposite effects. On the one hand, a progressive deactivation of the Lewis-acid sites, due to either the strong interaction of phenolics with the aromatic ring or the accumulation of water (the co-product in PB formation), causes the in situ transformation of the Lewis sites into Brønsted acid sites. On the other hand, under conditions of phenol scarcity (i.e., after 30%–40% phenol conversion), either the intramolecular rearrangement of PB into $o$-HBP might become kinetically preferred over the bimolecular reaction or an equilibration between the two isomers might lead the $p/o$-HBP selectivity ratio to approach a value close to the equilibrium one.

In the literature, the role of Lewis sites in acylation reactions is also highlighted; it is reported that P/W heteropoly salts or metal-exchanged clays are efficient catalysts for the acetylation of alcohols or of aromatic substrates, in which the reaction rate increases with the cation electronegativity. The reaction is initiated by the coordination of acetic anhydride to the metal cation, with polarization of the C–O bond in the coordinated species [102]. In our case, instead, the main effect of the Lewis acidity is on the selectivity ratio between the two HBP isomers.

Additional experiments carried out with PB as the reactant will help clarify the aspects related to the reaction network and to the role of acid sites.

2.3. Reactivity Experiments with PB

Figure 4 plots the selectivity to products obtained by reacting PB over the HB-38 zeolite, based on phenol conversion. Unexpectedly, HBP appeared to not be primary products of PB transformation, because their selectivity extrapolated at nil conversion was close to zero. This implies that the contribution of the intramolecular Fries rearrangement is negligible and that during phenol benzylation, the formation of HBP only occurs by means of the bimolecular reaction between PB and phenol. In the case of the reaction starting from PB, the intermolecular reaction may only occur between two PB molecules, to produce mainly $p$-BPB (selectivity to the ortho isomer was very low) and phenol. A further consecutive reaction between phenol and BPB or phenol and PB leads to the production of HBP isomers, with the coproduction of PB or phenol, respectively (however, in the latter case, the decrease in phenol selectivity shown in Figure 4 would not be justified). A rather similar trend was observed during PB reaction with HB-150.
The overall reaction network, as inferred from the experiments carried out starting from phenol and from PB, is shown in Scheme 1. Results suggest that differences shown among the H-beta samples are not due to the presence of various mechanisms for the transformation of phenyl benzoate into HBPs, but are instead attributable to the acidity features of the H-beta zeolites tested.

**Figure 4.** Phenyl benzoate (PB) reactivity: selectivity to main products based on PB conversion. Temperature: 190 °C.

**Scheme 1.** Reaction scheme for phenol benzylation with BA over H-beta zeolites.

2.4. The Reactivity of H-Y Zeolites

We tested the reactivity of three different commercial H-Y zeolites (Table 2). In regard to the acidity of H-Y, it is reported in the literature that Lewis acidity may also play an important role, even for samples having low Al content (see, for instance [103], and the references therein).

The results of catalytic experiments are shown in Figure 5. As can be seen, in all cases, phenol conversion was lower than that obtained with H-beta zeolites. If the initial conversion is taken into account, e.g., at a 0.25 h reaction time, the scale of activity was HY-7 > HY-3 > HY-100; thus, in this
case also, as with H-beta zeolites, the greatest activity was obtained with the intermediate SAR ratio. Overall, however, the activity was not much affected by the Si/Al ratio.

![Graphs showing phenol conversion and selectivity](image)

**Figure 5.** Phenol benzylation with BA: phenol conversion based on reaction time (A) and selectivity to phenylbenzoate (B), to \( p \)-hydroxybenzophenone (C), and \( o \)-hydroxybenzophenone (D) based on phenol conversion at \( T = 190 \) °C. (E): selectivity ratio between \( p \)- and \( o \)-hydroxybenzophenone. Catalysts: H-Y zeolites.

With these catalysts, also, PB was the only primary product, and the formation of HBPs occurred by the consecutive transformation of the ester. However, the selectivity to HBPs was lower than that shown with H-beta zeolites, even with the more active H-Y sample. Therefore, H-Y zeolites were also poorly efficient in the consecutive transformation of PB into HBPs; this is particularly apparent with the sample
HY-100, which showed a negligible consecutive transformation of PB into HBP, even at 30% phenol conversion. With all of the H-Y zeolites tested, no BPB formation was shown.

The lowest $p$-/$o$-HBP selectivity ratio was achieved with HY-100, the highest with H-Y samples having the greater Al content, which is the opposite of what was observed with H-beta zeolites; however, in this case also, the selectivity ratio seemed to approach a value close to one when the phenol conversion was increased.

Even when we changed the BA/phenol molar ratio (Figure 6), the highest overall selectivity to HBPs achieved was not higher than 32%. An excess of phenol, in experiments carried out at a BA/phenol molar ratio equal to 0.5 and 0.16, should be kinetically un conducive to an intermolecular transformation of PB to HBPs compared to a Fries-type rearrangement; therefore, we might expect a change in the $p$-/$o$-HBP ratio in the presence of both the inter- and intra-molecular mechanisms of PB transformation into HBPs. With experiments carried out using a BA/phenol molar ratio ≤1, the $p$-/$o$-HBP selectivity ratio was between 1.5 and 2.0, whereas in the case of the BA/phenol ratio of two, it was lower than 1.0.

![Figure 6](image)

**Figure 6.** Effect of the BA/Ph molar ratio on phenol (Ph) and benzoic acid (BA) conversion and selectivity to phenylbenzoate (PB) and hydroxybenzophenones (HBPs). Catalyst: HY-7, reaction time 4 h, $T = 190$ °C.

In order to gain more information on the reaction network, we conducted some experiments in which we reacted PB; we observed that the peak conversion of PB was reached with HY-3 (43%), the lowest with HY-100 (6%) and the intermediate value of 18% for HY-7. These results were in line with the PB selectivity decrease registered in phenol benzoylation experiments, during which PB underwent almost no consecutive transformation with HY-100. Surprisingly, however, no HBP was formed in these experiments, with the exception of some traces observed with the most active HY-3 compound. The only products found were phenol and BA. On the one hand, this indicates the presence of water in the zeolites (the greater amount being obviously shown with the more hydrophilic zeolite), which are responsible for the hydrolysis of the ester, but on the other hand, this suggests that both the intramolecular Fries rearrangement and the intermolecular reaction between two molecules of PB are slowed greatly under these conditions with H-Y catalysts.
It can be concluded that with H-Y zeolites, the presence of water (which is generated in situ during phenol benzylation tests) has a pronounced slowing effect on the rate of consecutive PB transformation into HPBs, thus explaining the lower selectivity to HBPs recorded with these catalysts. It is possible that Lewis acid sites, which play an important role in the reaction mechanism with H-beta, are strongly inhibited by the presence of water.

When we carried out the benzoylation of phenol with benzoic anhydride, a reaction that does not lead to the co-production of water, we obtained a greater phenol conversion, which is an expected result, because BA (the co-product in benzoylation with benzoic anhydride) is a more efficient leaving group than water (the co-product in benzoylation with BA). However, despite the greater phenol conversion achieved, the selectivity to HBPs still remained low (Figure 7); this indicates that the difference observed between H-beta and H-Y zeolites in phenol benzylation with BA was not due to water and to its interaction with Lewis acid sites.

**Figure 7.** Effect of the benzoic anhydride/Ph molar ratio on phenol (Ph) conversion and selectivity to phenylbenzoate (PB) and hydroxybenzophenones (HBPs). Catalyst: HY-7, reaction time 4 h, $T = 190 \, ^\circ\text{C}$.

Excellent performances in the benzoylation of phenol with benzoic anhydride were reported by Chaube et al. [19] with the use of an H-beta zeolite; the authors observed a $p$-/$o$-HBP selectivity ratio close to two, similar to that one also observed in our experiments with HY-7. However, a selectivity to HBPs as high as almost 70% at over 95% benzoic anhydride conversion could be obtained with the H-beta. Hoefnagel and Van Bekkum studied the acylation of resorcinol with benzoic acid, with H-beta in $p$-chlorotoluene solvent; a 70% yield to 2,4-dihydroxybenzophenone was reported, with 20% residual resorcinol monobenzoate [104]. Indeed, the better performance of H-beta in acylation of phenolics is well known and widely described in the literature, for example in the acylation of anisole with acetic anhydride (a process developed by Rhodia); however, acylation of veratrole is preferably carried out with H-Y zeolites [2].

Overall, we can state that despite both the large number of papers reporting on the use of zeolites for the acylation of phenolics (see Table 1) and the various interpretations advanced to explain the superior performance of one zeolite type over others, a clear picture as to the possible reasons for the
differences in the catalytic behavior for this reaction has not yet been produced. Furthermore, in our case, the better performance of H-beta zeolites over H-Y for HBPs’ production, notwithstanding the well-known analogies of H-BEA and H-FAU zeolite types, is difficult to explain, even though it is clearly attributable to a remarkably less efficient transformation rate of the intermediately-formed PB with H-Y. This difference is greater between samples having the lowest Al content, i.e., HB-150 and HY-100; in fact, the latter catalyst was substantially inactive in PB conversion into HBPs. Further studies are needed in order to develop a better understanding of the main zeolite characteristics that affect the catalytic properties in phenolic acylation.

3. Experimental Section

H-beta zeolites: commercial samples purchased from Zeolyst International (Conshohocken, PA, USA) (HB-38, HB-75 and HB-150) and from ZEOCHEM (Uetikon am See, Switzerland) (HB-13) were used. H-Y zeolites: commercial samples were purchased from TOSOH (Tokyo, Japan) (HY-3, HY-7 and HY-100).

Porosimetry was determined using a Micromeritics (Norcross, GA, USA) ASAP 2020 instrument. Thermal-programmed-desorption of ammonia (10% in He) was carried out using a TPDRO 1000 Thermo Finnigan Italia (Rodano, Italia) instrument. Samples were first pre-treated at 550 °C for 1 h; then, pulses of ammonia were fed onto the sample maintained at a temperature of 180 °C. The temperature was then raised (10 °C/min) up to 550 °C, and the sample was left at this temperature for 1 h, until the complete desorption of the ammonia.

FTIR spectra in the transmission mode were recorded after the adsorption of pyridine vapors under a vacuum on a self-supported thin film of the sample. The sample was initially pre-treated at 550 °C for 2 h; then, the cell was saturated with pyridine vapors at 100 °C, for 30 min. Lastly, the sample was heated at increasing temperatures, and the IR spectrum was recorded at defined temperature intervals.

In a typical benzoylation reaction, phenol (Sigma-Aldrich, St. Louis, MO, USA) (0.1 g), benzoic acid (Sigma-Aldrich, St. Louis, MO, USA) (0.13 g) (molar ratio phenol/benzoic acid = 1) and the catalyst (10 wt. % with respect to the reactants) were loaded without solvent in a sealed test tube equipped with a magnetic stirrer. The test tube was then placed in an oil bath and heated up to the temperature desired (190–200 °C). After the reaction, the crude was cooled, diluted with HPLC acetone, filtered and analyzed. The reaction mixture was analyzed with a Thermo Focus from Thermo Fisher (Waltham, MA, USA) GC gas-chromatograph equipped with an FID detector and Agilent (Santa Clara, CA, USA) HP-5 column, using \( n \)-decane as the internal standard. The analysis conditions were: 60 °C for 0 min, 40 °C/min up to 280 °C, 2 min at 280 °C.

4. Conclusions

Here, we report on the unprecedented reaction of phenol benzoylation with benzoic acid catalyzed by zeolites, which was carried out in the absence of solvent; this reaction is aimed at the production of hydroxybenzophenones, compounds of great interest for the chemical industry. H-beta zeolites offered a superior performance, in terms not only of activity, but also of selectivity to the desired compounds. The reaction network was found to consist of the primary reaction of phenol esterification with the formation of phenyl benzoate, which is then consecutively transformed into hydroxybenzophenones by
means of an intermolecular reaction between the ester and phenol; conversely, the contribution of the Fries rearrangement seemed to be negligible. With H-beta zeolites, the Si/Al ratio significantly affected performance, especially in terms of the selectivity ratio between the two hydroxybenzophenone isomers. An important role was played by Lewis-type acid sites, which were most abundant with Al-richer zeolites. Conversely, in the case of H-Y zeolites, the transformation of the ester into the desired ketones was greatly inhibited.

**Author Contributions**

G.G., S.P., F.B., P.M. and M.A. designed and performed experiments, and analyzed data. F.C. analyzed data and wrote the paper.

**Conflicts of Interest**

The authors declare no conflict of interest.

**References**


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