Subscriber access provided by ECU Libraries

Article

MIL-101 as reusable solid catalyst for autooxidation of benzylic hydrocarbons in the absence of additional oxidizing reagent

Andrea Santiago-Portillo, Sergio Navalon, Francisco G. Cirujano,
Francesc X Llabrés i Xamena, Mercedes Alvaro, and Hermenegildo Garcia

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.5b00411 • Publication Date (Web): 13 Apr 2015

Downloaded from http://pubs.acs.org on April 19, 2015

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

ACS Catalysis is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

MIL-101 as reusable solid catalyst for autooxidation of benzylic hydrocarbons in the absence of additional oxidizing reagent

Andrea Santiago-Portillo,[†] *Sergio Navalón,*[†] *Francisco G. Cirujano,*[†] *Francesc X. Llabrés i Xamena,*[†] *Mercedes Alvaro,*[†] *Hermenegildo Garcia,*[†,§,*]

[†] Departamento de Química and Instituto de Tecnología Química CSIC-UPV, Universidad Politécnica de Valencia, Consejo Superior de Investigaciones Científicas, Av. de los Naranjos s/n, 46022 Valencia, Spain

[§] Center of Excellence for Advanced Materials Research, King Abdulaziz University, Jeddah, Saudi Arabia

KEYWORDS: heterogeneous catalysis, metal organic frameworks, aerobic oxidation, MIL-101 as catalyst, benzylic oxidation

ABSTRACT. MIL-101 promotes benzylic oxidation of hydrocarbons exclusively by molecular oxygen in the absence of any other oxidizing reagent or initiator. Using indane as model compound, the selectivity towards the wanted ol/one mixture is higher for MIL-101(Cr) (87 % selectivity at 30 % conversion) than for MIL-101(Fe) (71 % selectivity at 30 % conversion), a fact that was associated to the preferential adsorption of indane within the pore system. Product distribution and quenching experiments with TEMPO, benzoic acid and dimethylformamide show that the reaction mechanism is a radical chain autooxidation of the benzylic positions by molecular oxygen and the differences in selectivity have been attributed to the occurrence of the autooxidation mostly process inside or outside the MOF pores. MIL-101 is reusable, does not leach metals to the solution, and maintains the crystal structure during the reaction. The scope of the benzylic oxidation was expanded to other benzylic compounds including ethylbenzene, *n*-butylbenzene, iso-butylbenzene, 1-bromo-4-butylbenzene, *sec*-butylbenzene and cumene.

INTRODUCTION

Metal organic frameworks (MOFs) offer many opportunities as heterogeneous catalysts, particularly for liquid-phase organic reactions.[1-12] One of the most challenging organic reactions is oxidation of hydrocarbons by molecular oxygen.[13-16] This type of reactions are carried out in large industrial processes under homogeneous conditions using sometimes metal acetates in which the metal center can have a similar coordination sphere as in MOFs having carboxylate linkers. In a series of papers we have reported that commercially available Fe-BTC (BTC: benzene tricarboxylate) is unable to promote aerobic oxidations of alcohols and hydrocarbons in the absence of co-promoters.[5] However, if Fe-BTC contains N-hydroxyphthalimide (NHPI)[17] or Cu-BTC 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO),[18] then, the resulting solids have activity for various aerobic oxidations[5] in a similar way as the combination of Co^{2+}, Mn^{2+} and other transition metals with NHPI in homogeneous phase.[19-21] Considering the importance of aerobic oxidations in the chemical industry and continuing with this line of research it would be of interest to develop more efficient systems in which aerobic oxidation can take place in the absence of any co-catalyst. Herein we report that MIL-101(Cr) or MIL-101(Fe) (MIL-101:

Materieaux de l'Institute Lavosier) are able to trigger benzylic oxidation of hydrocarbons by oxygen in the absence of any co-promoter.

In the literature there are some precedents reporting the use of MOFs for oxidation of cycloalkanes,[22] alkenes,[23-27] benzylic positions,[28-31] or epoxidation of styrene,[32] but, so far these studies have commonly used hydroperoxides such as *tert*-butylhydroperoxide (TBHP)[22-25,28,31-33] as oxidizing reagents. In a few scattered precedents peroxides such as H_2O_2[26,32] or trimethylacetaldehyde with oxygen[27] to generate acylperoxy radicals have been used instead of organic hydroperoxides. Similarly, the combination of organic peroxides as initiators, Fe- or Cr-based MIL-100 or MIL-101 as catalyst and O_2 as reagent has been reported for the oxidation of cyclohexane [22] or alkenes (cyclohexene, α- or β-pinene and limonene).[24,34,35] However, the exclusive use of molecular O_2 to promote the oxidation using MOF as initiators has remained as far as we know unexplored. In this context, it would be important if this process could be carried out in the total absence of any hydroperoxide as reagent or initiator and only molecular oxygen and MOFs is used.[32,36,37] In the present article we report that MIL-101(Cr) or MIL-101(Fe) in the presence of oxygen are able to activate the autooxidation of benzylic hydrocarbons with a selectivity that is higher than that achieved for the same conversion with conventional radical initiators.

RESULTS AND DISCUSSION

In the first stage of our work we selected indane as model substrate and tested the catalytic activity of MIL-101(Cr) and MIL-101(Fe) before and after activation at 120 ºC under vacuum for 6 h. The purpose is to determine the influence that co-adsorbed DMF/ethanol or water can have on the catalytic activity of the material. Precedents in the literature have shown that water is removed from MIL-101 upon activation at 120 °C under vacuum.[22,35] Table 1 shows the BET surface area and pore volume of MIL-101(Cr) and MIL-101(Fe) as a function of the activation temperature. As it can be seen there, the surface area and porosity increases along the pretreatment temperature in the range from 80 to 140 ºC, following similar trend both MIL-101 samples.

Table 1. Surface area and pore volume of the MIL-101(Cr) and MIL-101(Fe) samples used in the present work as a function of the activation temperature.

	Activation temperature (ºC)	BET (m^2/g)	Pore volume (cm^3/g)
MIL-101(Cr)	80	1765	1.14
	140	2014	1.18
MIL-101(Fe)	80	1834	0.98
	140	2058	1.19

In all cases, conversion of indane with predominant formation of the expected benzylic -ol/-one products was observed. A control experiment under the reaction conditions in the absence of any catalyst shows up to 10 % indane conversion. This conversion in the absence of catalyst corresponds according to the literature [38,39] to the inefficient occurrence of some degree of thermal autooxidation in which O_2 forming collisional charge transfer complexes with aromatic ring generates the first $O_2^{-\cdot}$ superoxide that triggers some aerobic oxidation. In contrast, autooxidation occurs in much higher degree in the presence of MIL-101 as initiators (see Figure 1a). The possibility that in the experiments using MIL-101 as initiator, indane sample contained some hydroperoxide formed by aging of indane in contact with the atmosphere was considered and dismised by distilling sample immediately before using it and observing almost coincident time-conversion plots (maximal lower difference for the distilled sample 2 %) for the freshly distilled sample (see Figure S2).

Comparison of the catalytic activity of materials without (Figure S3) and after activation (Figure 1) showed MIL-101(Cr) has very similar time conversion plots with and without activation treatment while, in contrast, a significant increase in the catalytic activity of MIL-101(Fe) was observed after activation. To illustrate the catalytic activity, Figure 1 shows time conversion plots for indane in the presence of activated MIL-101 catalysts. These preliminary tests lead to the conclusion that MIL-101(Cr) without any thermal treatment is a convenient catalyst for benzylic autooxidations, in view of its high (-ol/-one) selectivity, especially at indane conversions below 50 %. Thus, for the following experiments MIL-101(Cr) was used without pretreatment. Interestingly, while the ol/one selectivity decreases as indane conversion increases for MIL-101(Cr), in the case of MIL-101(Fe) maximum in the selectivity was observed at about 50 % conversion (Figure 1b and S3b). This enhancement of ol/one selectivity at low conversion is probably due to the decomposition of hydroperoxide to the ol/one in this range of conversions (Figure 1c and S3c).

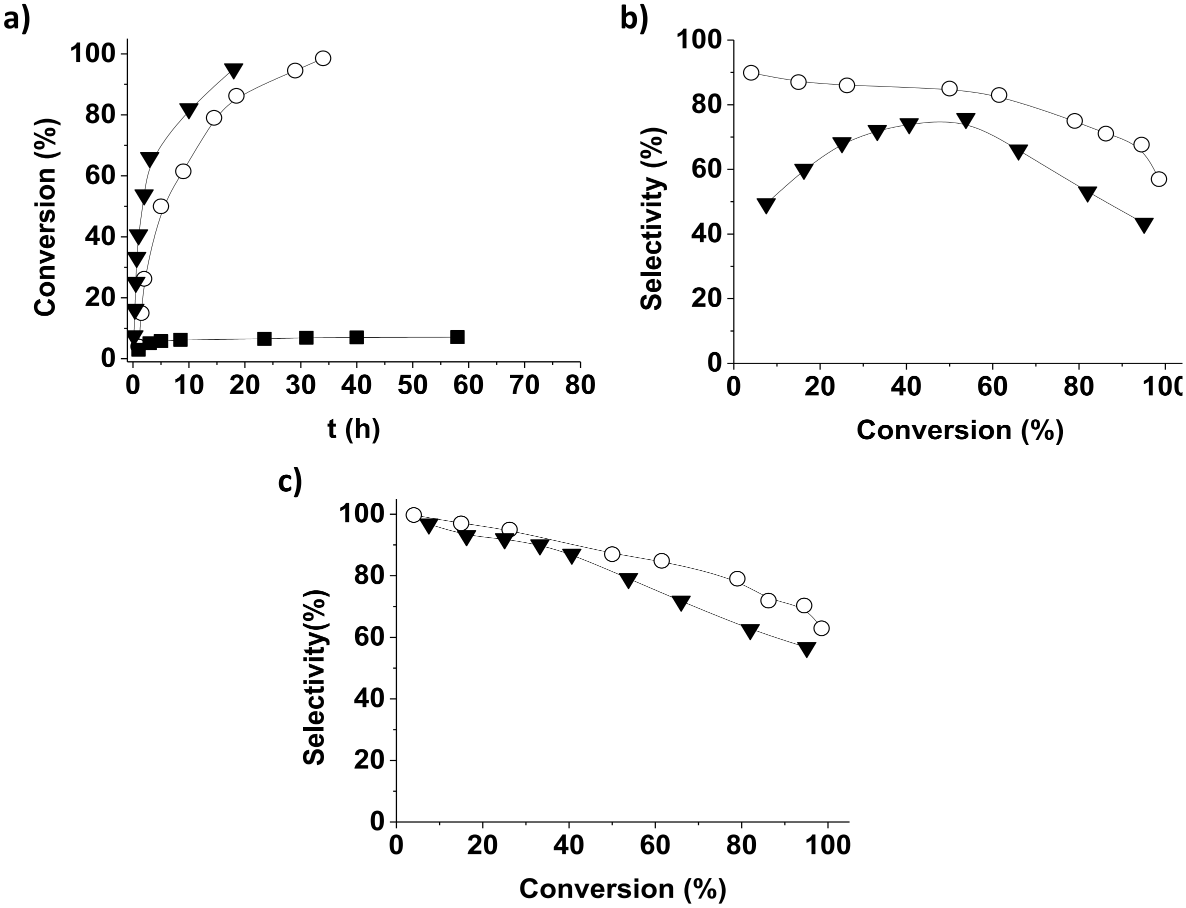
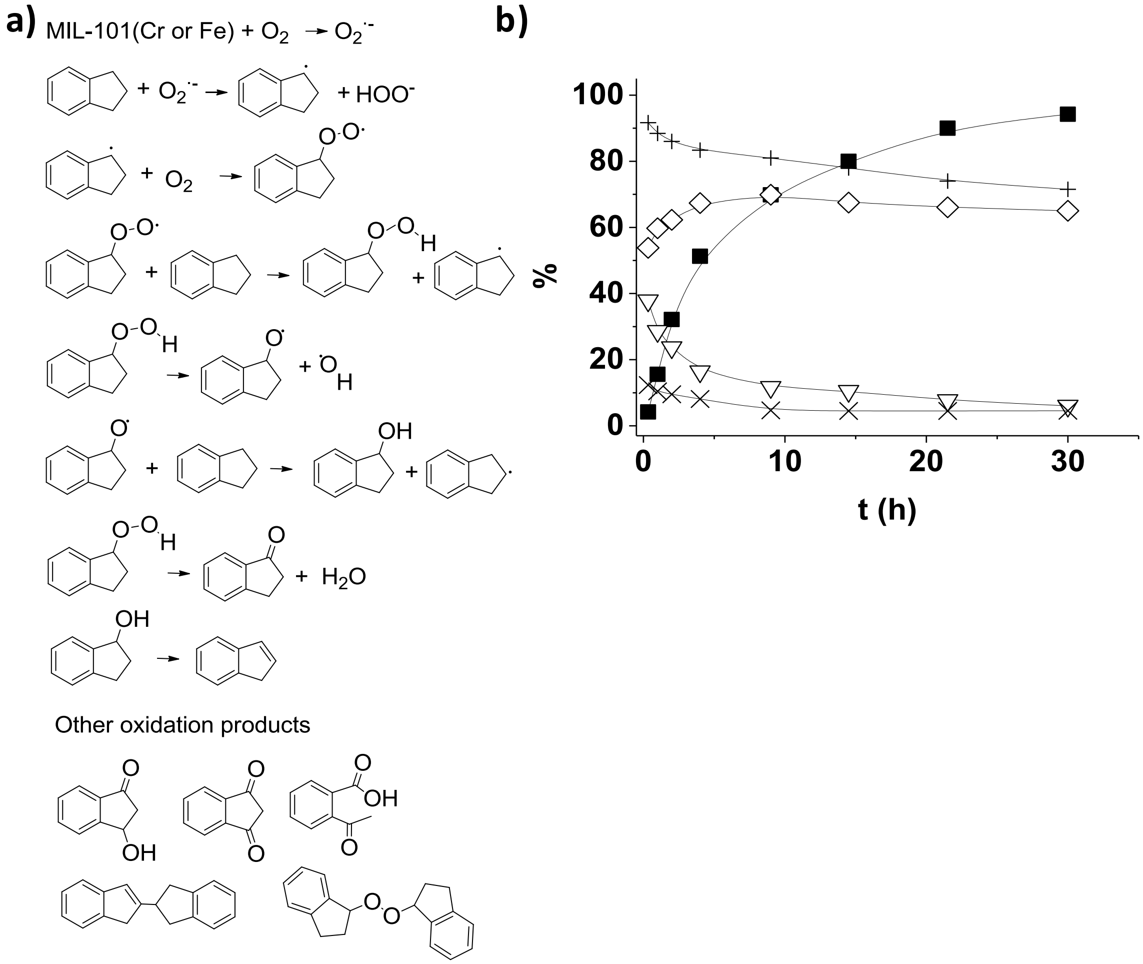


Figure 1. Time conversion plot (a), selectivity(-ol/-one)-conversion plot (b) and selectivity(-ol/-one plus hydroperoxide)-conversion plot (c) for the aerobic oxidation of indane using activated MIL-101(Cr or Fe) as catalysts. Legend: MIL-101(Fe) (▲); MIL-101(Cr) (○); Blank control in the absence of catalyst (■). Reaction conditions: 75 mg catalyst, 20 mmol substrate, 120 ºC, O_2 atmosphere.

Scheme 1 shows the products observed for indane oxidation and the proposed reaction pathway (a) based on the temporal variation of the product distribution (Scheme 1b and Figure S1). As it can be seen in this Scheme the corresponding 1-indanol/one appear as unstable products that undergo further oxidation as the reaction time increases. The ol/one mixture would derive from the corresponding indanyl-1-hydroperoxide, that was characterized by GC-FID after decomposition with $P(Ph_3)_3$.[40] It is known that organic hydroperoxides can decompose giving the corresponding alcohol and ketone in variable amounts depending on the reaction conditions.[39,41] Mass balances in the catalytic oxidation of indane using MIL-101(Cr) or MIL-101(Fe), based on the initial indane moles, were in all cases higher than 95 % although we notice that mass balances tend to decrease slightly along the conversion.



Scheme 1. (a) Proposed reaction pathway for the oxidation of indane using MIL-101(Cr or Fe) as catalyst and (b) time conversion and product selectivity plot for the oxidation of indane using unactivated MIL-101(Cr). Legend: Indane conversion (■) and selectivity to 1-indanyl hydroperoxyde (x), indanone (◊), indanol (∇) and indanol+indanone (+). Reaction conditions: 75 mg MIL-101(Cr), catalyst, 20 mmol substrate, 120 ºC, O_2 atmosphere.

To put into context these preliminary catalytic tests it should be noted that studies in the literature have shown than while similar activation treatments are able to reduce a significant population of Fe(III) ions to Fe(II),[42-44] in the case of MIL-101(Cr) no such change in the oxidation state is observed.[45] Note that when a Fe(III) is reduced to Fe(II), one of the apical -OH ligands initially bound to the metal ion is lost to keep the electrical neutrality of the system, thus becoming more exposed and available for oxygen activation. Apparently, the catalytic data indicate that the presence of Fe(II) is in principle beneficial for the activity of MIL-101(Fe). We will come back to this point when discussing the oxidation mechanism.

Related to the different reactivity of MIL-101(Cr) or MIL-101(Fe), transition metal chemistry shows that even for a given oxidation state, the reactivity of metal complexes is dependent on the nature of the cation.[45,46] In the present case, it should also be noted that due to the different conditions of the synthesis, MIL-101(Cr) has F^- ions, while MIL-101(Fe) has Cl^- ions. These differences have to be responsible for the higher catalytic activity of MIL-101(Cr) with respect to MIL-101(Fe).

One of the main problems of aerobic oxidations is the lack of product selectivity that decreases along conversion. From the conversion-selectivity plot for indane oxidation shown in Figure 1b MIL-101(Cr) exhibits, in spite of having the same structure, higher selectivity than MIL-101(Fe). Moreover, for conversions below 50 % -ol/-one selectivities higher than 85 % were attained over MIL-101(Cr). A possible rationalization for this higher selectivity ((indanol+indanone)/indane ratio) is based on the assumption that the reaction is taking place mainly inside the MOF pores. In this case the pores of MIL-101(Cr) should favor adsorption of indane and desorption of the more polar -ol/-one products. Thus, the preferential adsorption of indane inside the pores would make more favorable its oxidation over secondary oxidation of more polar -ol/-one products.

To provide experimental support to the preferred adsorption of indane versus indanol/indanone in MIL-101(Cr) respect to MIL-101(Fe), isothermal adsorption measurements of indane, indanol and indanone as well as mixture of these products were performed and a summary of the results is presented in the Supplementary Information (Table S1). It was determined that the adsorption ratios indane/indanol, indane/indanone or indane/(indanol+indanone) are higher in the adsorption experiments of MIL-101(Cr) with respect to MIL-101(Fe), thus, lending support to differences in adsorption preferences as the possible origin of the selectivity differences observed for both MOFs. In addition, it could be that these differences could derive from the different 1-indanyl hydroperoxide stability in both MOFs (compare Figures 1b and 1 c, S3b and 3Sc) as consequence of the higher ability of Cr^{3+} to decompose this intermediate as compared to $Fe^{2+}/^{3+}$ ions.[47,48]

Stability of MIL-101(Cr) as catalyst was determined by measuring the catalytic activity upon consecutive reuses as well as by analytical measurements of ion metals in the solution and by determining the crystallinity of the solid. It was observed that in four consecutive uses the time conversion plot (Figure 2a) and the conversion/selectivity curve (Figure 2b) were coincident, thus proving that the catalytic activity does not decrease upon reuse. Furthermore, ICP-AES chemical analysis of Cr in the liquid phase showed that the content of this metal is less than 0.2 % of initial amount of this element in the catalyst. Also, XRD of MIL-101(Cr) shows that the crystallinity of the solid is preserved in four reuses (Figure 2c). Overall these three consistent pieces of evidence support the stability of the MIL-101(Cr) as catalyst. Similarly, it was found that powder XRD of MIL-101(Fe) does not change upon its use as catalyst (Figure 2d) and that the Fe leaching measured by ICP AES was 1.6 wt% of the initial total amount of Fe present in MIL-101(Fe). This stability is not surprising considering that MIL-101 is one of the most robust

MOFs that can stand without deterioration treatments under harsher conditions than those employed here.[49] Also the higher Fe leaching compared to Cr suggesting the higher stability of MIL-101(Cr) with respect to MIL-101(Fe) has been previously observed by Kholdeeva and co-workers, when they used these materials as catalysts for the solvent-free allylic oxidation of alkenes with O_2 and small amounts of TBHP as radical initiator.[24,35]

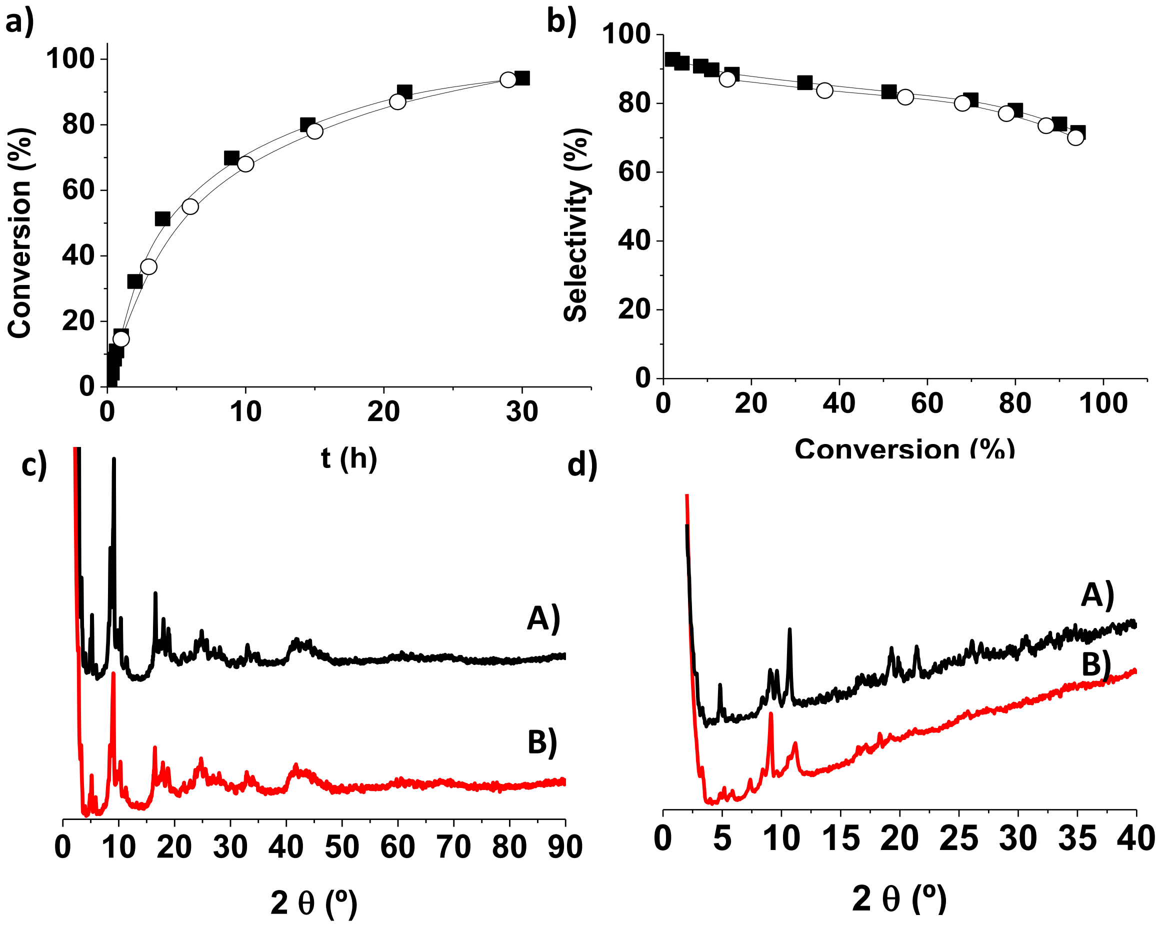


Figure 2. (a,b) Reusability of MIL-101(Cr) as catalyst for the aerobic oxidation of indane, (c) crystallinity of the fresh MIL-101(Cr) (A) and after four uses (B) and (d) XRD of fresh MIL-101(Fe) (A) and after its use (B) as catalyst for indane aerobic oxidation. Legend: 1st use (■) , 4th use (○). Reaction conditions: 75 mg catalyst, 20 mmol substrate, 120 ºC, O_2 atmosphere.

Heterogeneity of the reaction was studied by performing hot filtration tests. The results presented in Figure 3 showed, however, that the temporal profile in the indane conversion is almost unaffected by removal of the solid. However, the selectivity (-ol/-one) of the filtrate is lower than that in the presence of MIL-101(Cr). A similar result in the hot filtration test has been observed for the oxidation of tetralin to 1-tetralone using TBHP as oxidant, MIL-101(Cr) as catalyst and chlorobenzene as solvent.[29] In this precedent, the slight increase of tetralin conversion after catalyst filtration was attributed to the thermal autooxidation of tetralin due to the presence of active radical intermediates in the filtrate and the very low Cr leaching (0.14 ppm) from MIL-101(Cr). In addition, a lower selectivity value towards 1-tetralone after catalyst filtration (73 %) respect to the selectivity (83 %) in the presence of catalyst was also observed.[29] Similarly, other work dealing with the solvent-free aerobic oxidation of tetralin using a Cu-MOF also proposed that the conversion evolution after catalyst removal was mainly due to the presence of organic hydroperoxides that are involved in the thermal autooxidation of tetralin.[36] To support this proposal and considering the very small amount of Cr leaching measured for the experiment using MIL-101(Cr), a control experiment in which indane autooxidation was promoted by $Cr(CH_3COO)_3$ in a concentration corresponding to the amount determined to leach from MIL-101(Cr) was carried out (Figure S4). It was observed that this minute amount of Cr^{3+} (0.00058 mmol) was able to promote indane autooxidation in a significant extent up to 78 % in 30 h, although the ol/one selectivity for the control using $Cr(CH_3COO)_3$ was significantly lower than that achieved in the presence of MIL-101(Cr) as initiator (see Figure S4).

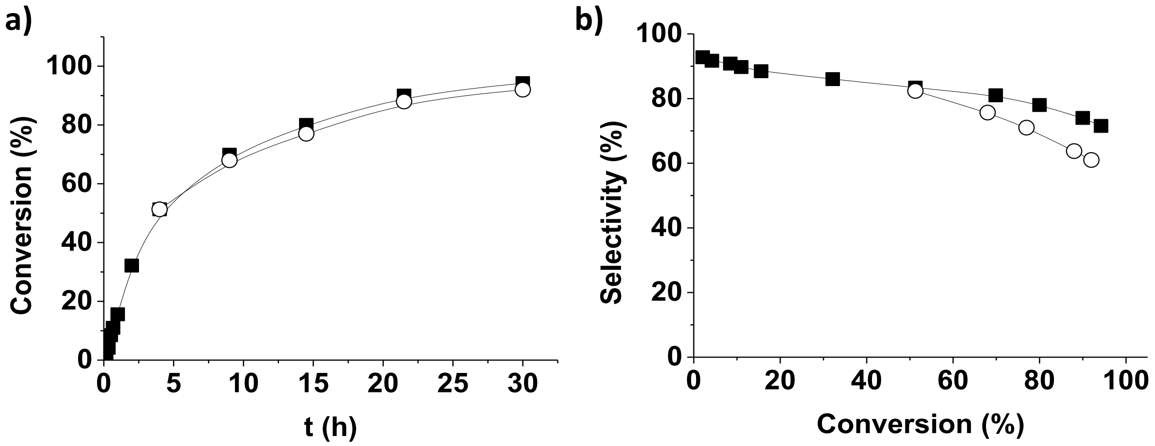


Figure 3. Time-conversion (a) and selectivity (-ol/-one)-conversion (b) plots for the oxidation of indane in the presence of MIL-101(Cr) (■) and after filtering the catalyst at 50 % conversion (○). Reaction conditions: 75 mg catalyst, 20 mmol substrate, 120 ºC, O_2 atmosphere.

In our case, this lack of influence of the presence of solid once the reaction has started would be compatible with two scenarios, either the occurrence of leaching with catalytically active species present in liquid phase or with the operation of an autooxidation mechanism for the reaction. We have already commented that chemical analysis shows conclusively that the percentage of metal leaching in the solution is negligible and, therefore, we suggest that the role of MIL-101(Cr) in the aerobic oxidation of indane is to act as an initiator of a radical chain mechanism with a long chain cycle. In other words, once C-centered benzylic radicals are formed in the presence of oxygen, a chain oxidation can take place not only in the pores of the solid, but also in the liquid phase in the absence of solid. This chain mechanism of indane autooxidation occurring even in the absence of MIL-101 requires the presence of (hydro)peroxides that are detectable by GC analysis. In order to provide evidence of the presence of indanyl hydroperoxide in the reaction mixture we use the conventional procedure in which an excess amount of triphenylphosphine is added to the reaction mixture and the formation of triphenylphosphine oxide, generated by nucleophilic decomposition of organic hydroperoxide, quantified by GC.[40] Equation 1 indicates the process through which indirect quantification of unstable hydroperoxides can be determined by triphenylphosphine. The results obtained show, in fact, that depending on the reaction time various concentrations of hydroperoxide accounting up to 12 % of selectivity at 25 % indane conversion can be present in the reaction mixture (plot of Scheme 1b).

$$\text{R-OOH} + (\text{Ph})_3\text{P} \rightarrow \text{R-OH} + (\text{Ph})_3\text{PO} \quad (\text{Eq. } 1)$$

To support the role of MIL-101 solids as initiators of long chain autooxidation mechanism, we performed a series of experiments in which TBHP (Figure 4a,c and S5a,c) or azobisisobutyronitrile (AIBN) (Figure 4b,d and S5b,d) as radical initiators were used as autooxidation promoters in the absence of any solid. The amount of TBHP or AIBN was the same as the moles of metal present in the MIL-101(Cr) solid (0.29 mmol) or the moles of 1-indanylhydroperoxide found in the reaction mixture (0.6 mmol) using MIL-101(Cr) as catalyst. Using these organic radical initiators, conversion of indane is higher using AIBN with respect to the use of MIL-101(Cr), while similar conversions were found when using TBHP as radical initiator. The main difference, however, between the use of AIBN or TBHP and MIL-101(Cr) is the product selectivity that for the whole range of conversions is always lower for -ol/-one products with organic radical initiators than MIL-101(Cr) that is the most selective solid or even than MIL-101(Fe). For instance, in neat indane at 30 % conversion the selectivity of ol/one mixture using AIBN as radical initiator is 66 %, using TBHP is 74 % and in MIL-101(Cr) is 87 %. It should be noted that in aerobic oxidations, selectivity is the key parameter, rather than conversions. Due to the complexity of the reaction mixtures in aerobic oxidations, product purification is a costly process and it is generally preferred to perform oxidations at lower conversions in order to have high selectivity. In this regard, the performance of MIL-101(Cr) is notably better than that of organic radical initiators. Using chromium acetate as homogeneous catalyst for the aerobic oxidation of indane resulted in a selectivity to -ol/one of 69 % at 30 % conversion (Figure S3). These values confirm the superior performance of MIL-101(Cr) in terms of control of the product distribution of the aerobic oxidation.

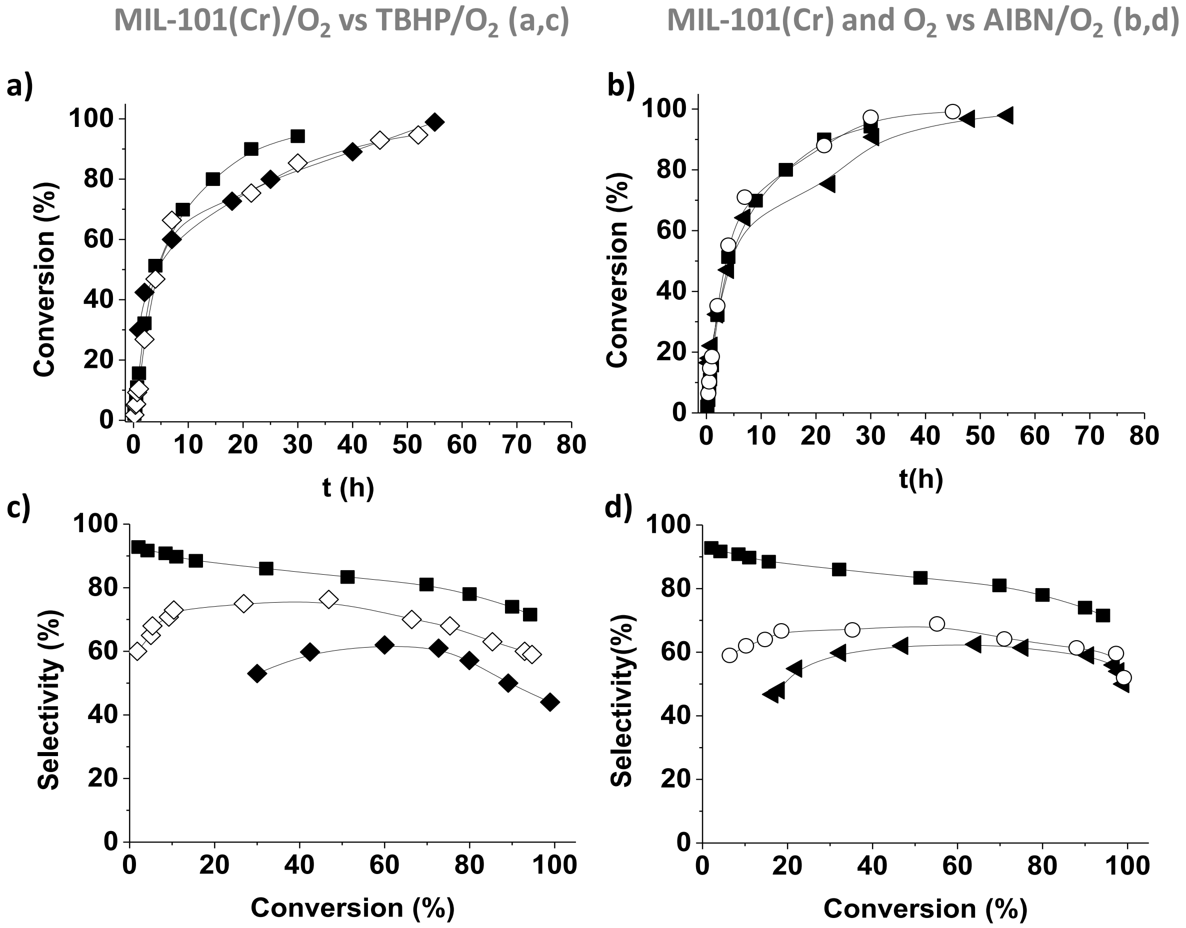


Figure 4. Time conversion (a,b) and selectivity (-ol/-one)-conversion (c,d) plots for aerobic oxidation of indane in the presence of MIL-101(Cr) as heterogeneous catalyst and O_2 (■; 75 mg, 0.29 mmol Cr) and the homogeneous organic radical initiators TBHP (◊, 0.15 mmol; ♦, 2 mmol.) and AIBN (○, 0.15 mmol; ◀, 0.5 mmol). Reaction conditions: MIL-101(Cr) or oxidant as indicated, 20 mmol substrate, 120 ºC, O_2 atmosphere.

Thus, apparently the main role of MIL-101 in the presence of oxygen is to act as radical initiator and to provide reaction cavities with different compound concentration and different polarity than the liquid phase. The activity of MIL-101 solids as radical initiators together with long propagation chain of indane autooxidation can explain that once the radicals have been generated, filtration of the solid does not affect to the conversion but only to the product se4lectivity (Figure 3). The role of MIL-101 solids as radical initiators was supported by kinetic measurements in which the amount of solid was varied over one order of magnitude from 75 to 7.5 or 1.5 mg without observing variation on the initial reaction rate and temporal profile of indane disappearance (Figure 5a), although selectivity as a function of the amount of catalyst revealed variations in the relative proportions of the processes taking place inside and outside the pores (Figure 5b) (compare selectivity plots of Figures 5b and S6).

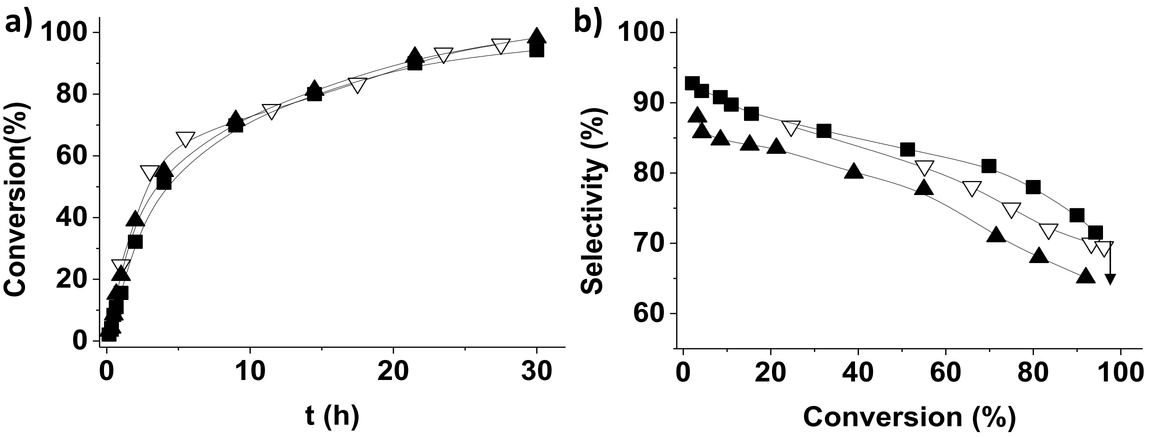


Figure 5. Time-conversion plot (a) and selectivity (-ol/-one)-conversion (b) for the aerobic oxidation of indane using different catalyst amounts. Legend and reaction conditions: Unactivated catalyst amount [75 mg (■), 7.5 mg (∇) or 1.5 mg (▲)], 20 mmol indane, 120 ºC, O_2 atmosphere.

This would indicate that only a few indanyl radicals are being formed by the solid catalyst. The substrate conversions and, therefore, the reaction rate is controlled not by the initiation step but by the propagation rate that basically depends on oxygen concentration and the chain length. If instead of oxygen, air is used in the process a significant decrease on the initial reaction rate, following the expected trend for first order kinetics with respect to oxygen pressure was determined (Figure 6 and Figure S7). As it can be seen in Figure 6 when the experiment is carried out in the absence of oxygen indane conversion does not occur, but if the reaction is started under Ar and then O_2 is admitted into the system, then, the same reaction rate as for the reaction initiated under oxygen is observed.

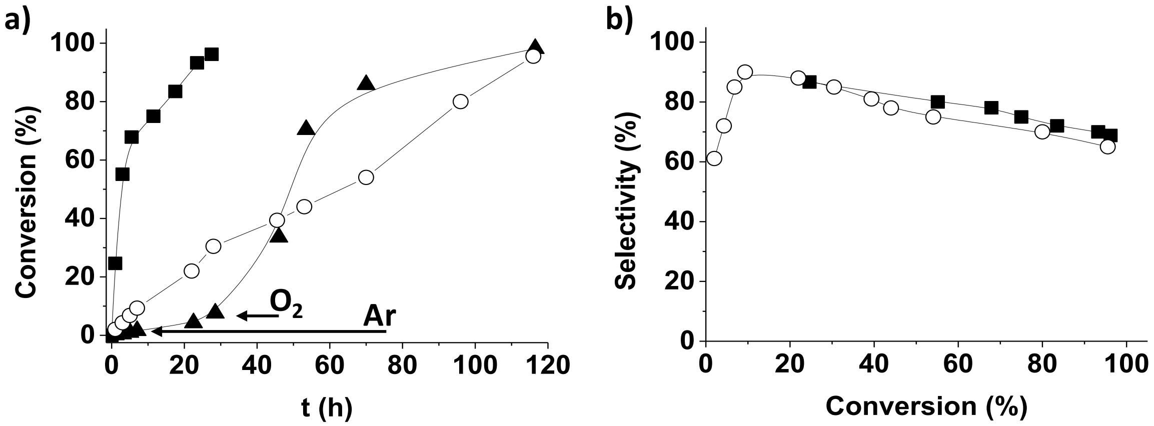


Figure 6. Influence of the reaction atmosphere on the time-conversion plot (a) and selectivity (-ol/-one)-conversion (b) during the indane reaction in the presence of MIL-101(Cr). Legend: O_2 (■), air (○), Ar for 23 h and then O_2 (▲).

In order to provide additional information about the oxidation pathway a series of experiments shown in Figure 7 in which indane oxidation was performed with MIL-101(Cr) in the presence of TEMPO, benzoic acid and DMF were performed. It was observed that while TEMPO (either added at the initial time or added at 1.5 h of reaction time corresponding to 28 % indane conversion) efficiently inhibits the reaction, the presence of benzoic acid has no influence on the catalytic activity. Also, DMF act as inhibitor of the aerobic oxidation of indane. These results of the influence of the presence of quenchers in the reaction indicate that acid/base sites are probably not involved in the oxidation, while the most likely reaction intermediates involve benzylic radicals. In fact, when TEMPO is present, simultaneously to O_2, the product distribution change somewhat and symmetric and asymmetric peroxides of indanyl and indenyl, together with some 1-indanyl ethers were characterized in the reaction mixture. TEMPO and DMF are able to quench the reaction either added at the initial time (Figure 7) or added once the reaction has already been initiated (Figure S8).

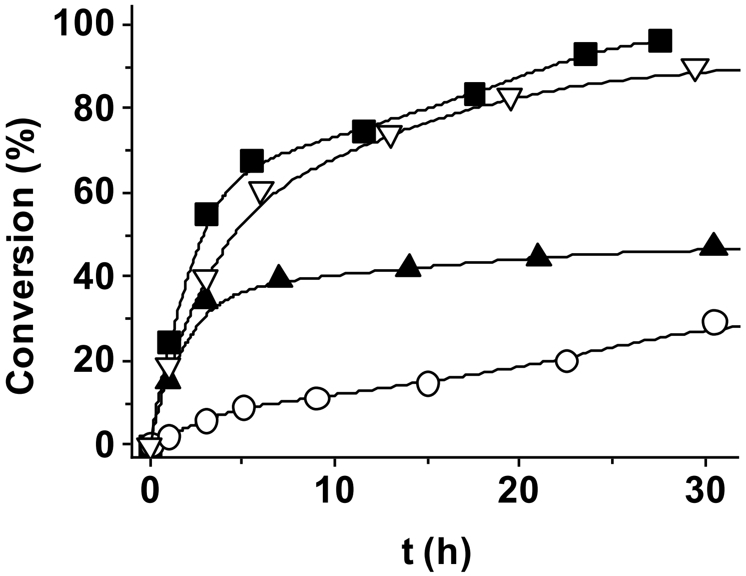


Figure 7. Aerobic oxidation of indane using MIL-101(Cr) as catalyst (■) in the presence of TEMPO (○), benzoic acid (∇) and DMF (▲). Reaction conditions: 75 mg catalyst, indane (20 mmol), O_2 atmosphere, 120 ºC.

This proposal of MIL-101 solids acting as radical initiators also agrees with the fact that the productivity test in which larger excess of indane is being converted (460 and 444 mmoles in the first and second use) by MIL-101(Cr) (1.5 mg) (Figure S6). Under these conditions in which a large excess of indane over MIL-101(Cr) is used the reaction eventually stops at long reaction times reaching conversions of about 85 % without reaching complete conversions. This behavior would be consistent with reversible catalyst deactivation, in the present case, due to the lack of ability to generate benzylic radicals. However, if the solid catalyst is recovered by filtration and exhaustively washed with ethanol and then reused very similar temporal profile as the one determined for the fresh material is again observed. Therefore, the apparent catalyst deactivation is caused by blocking of the active sites by reaction products rather than by a deterioration of the active sites that recover their activity upon removal of those reaction products acting as poisons.

In order to expand further the scope of MIL-101 as radical initiator promoting autoxidation of benzylic hydrocarbons, we screened the oxidation of six different compounds, namely ethylbenzene, *n*-butylbenzene, isobutylbenzene, cumene, *sec*-butylbenzene and 1-bromo-4-butylbenzene. These experiments (except ethylbenzene that was always distilled) were carried out using both undistilled and freshly distilled substrates. The aim of these experiments was to determine whether or not the possible presence of a minor amount of organic hydroperoxide in aged samples could influence the catalytic activity when using MIL-101(Cr) as catalyst (Figure S9-S19). It was observed that the catalytic activity using distilled substrates is similar or slightly lower (difference less than 5%) than that observed using undistilled substrates and, therefore, the observed catalytic activity was mainly due to the formation of radical species arising from the interaction of the metal cluster in the MIL-101 with molecular O_2 (see below). In all cases, full conversion of the starting material promoted by MIL-101(Cr) to a range of products that can be easily rationalized as derived from autooxidation at the benzylic position were determined. Table 2 provides a summary of the results obtained while Figures S9-S19 illustrate the kinetics of the processes. As a general trend, ethylbenzene and *sec*-butylbenzene give rise to the formation of acetophenone whose selectivity is maintained during the conversion of the hydrocarbon. In contrast, *n*-butyl and isobutylbenzene form as primary product the corresponding butyrophenone that appears as unstable during the course of the reaction, undergoing further oxidation to benzoic acid. This instability of butyrophenone with respect to acetophenone reflects the different ability to undergo oxidative C-C bond cleavage of a methyl group (case of ethylbenzene and *sec*-butylbenzene) with respect to the easier reactivity of methylene groups (butyrophenone). The fact that the reaction intermediate would be the corresponding benzyl radical is supported by the fact that a bromo substituent in the *para* position decreases the reaction rate by a factor of about 1.2 that agrees with the expected influence of a *p*-bromo electron withdrawing group as substituent. Tertiary benzylic radicals, like cumyl radicals, form more stable hydroperoxides that can be quantified in this case by GC and GC-MS. It was found that selectivity to the hydroperoxide decreases with cumene conversion as is known for oxidations promoted through radicals.

Table 2. Aerobic oxidation of aromatic benzylic hydrocarbons using MIL-101(Cr) as catalyst.[a]

	Conversion (%)	Main reaction products	Selectivity (%)
Ethylbenzene	90	Acetophenone	80
n-Butylbenzene[b]	100	Benzoic acid Butyrophenone	58 40
Isobutylbenzene[c]	100	Benzoic acid Phenylisopropyl ketone	78 18
Cumene	100	Acetophenone Cumyl hydroperoxide	78 18
sec-Butylbenzene	100	Acetophenone Propiophenone	79 18
1-Bromo-4-butylbenzene	50	4-bromobutyrophenone	80

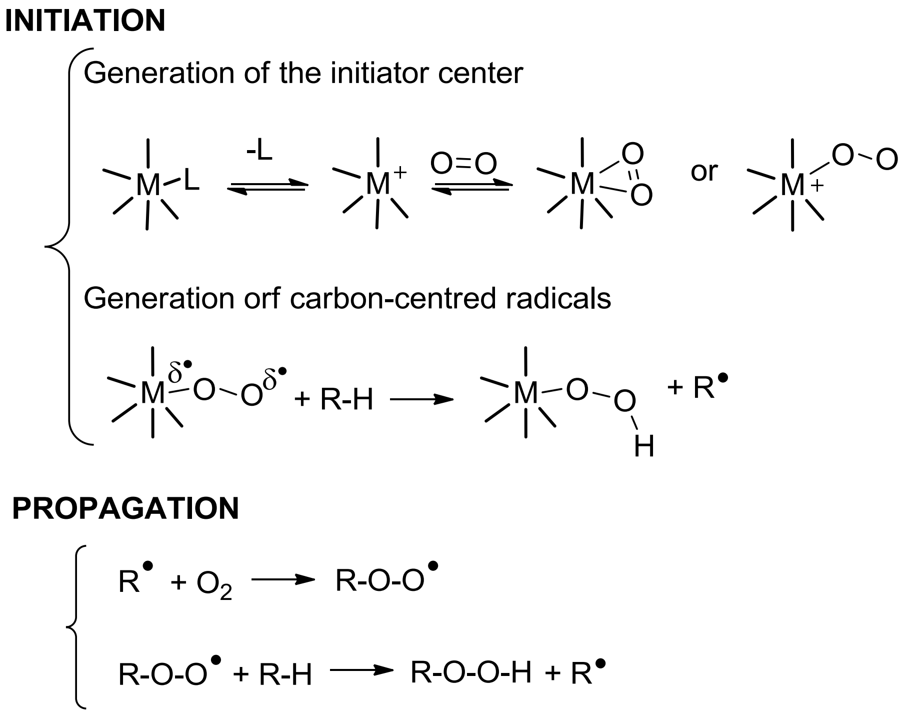
[a] Reaction conditions: 7.5 mg catalyst, 20 mmol substrate, O_2 atmosphere, 120 ºC and reaction time as indicated in Figures S7 to S17.

[b] Reaction time 96 h

[c] Reaction time 46 h

In order to highlight the influence of the MIL-101(Cr) porous structure on the reaction outcome, i.e. the possible operation of size-selective or a shape-selective catalysis), the catalytic activity as substrate of cumene or 1,3-diisopropylbenzene was compared for the aerobic oxidation. Figure S20 clearly shows the lower conversion for 1,3- diisopropylbenzene compared to cumene, in spite that the former contains two isopropyl groups. This lower reactivity of 1,3-diisopropylbenzene can be attributable to its lower diffusion through the MIL-101(Cr) pores due to its larger molecular dimensions compared to cumene and that the radical chain oxidation reaction takes place preferentially inside MIL-101(Cr) pores. If superoxide or other reactive oxygen species were able to diffuse outside the solid and most of the oxidation were taking place outside the crystal, then, no difference between cumene and 1,3-diisorpropylbenzene should be expected. The occurrence of oxidation preferentially inside the pores was further supported by performing isothermal adsorption experiments and observing a higher preferential of absorption in the MIL-101(Cr) of cumene (0.077 mmol/75 mg) than that obtained using 1,3-diisopropylbenzene (0.033 mmol/75 mg). In addition, a study of the influence of the reaction temperature on the cumene and 1,3-diisopropylbenzene conversion gives apparent activation energy values of 18.6 and 19.5 kcal mol^{-1} that indicate that the reactions are really under kinetic control (Figure S21). **It should be noted that in general reactions controlled by diffusion have activation energies below 5 kcal mol^{-1}.**

The present data on the catalytic activity of MIL-101(Cr) or MIL-101(Fe), differing in the relative adsorption preference can be put into context with the failure of commercial Fe-BTC to promote this type of oxidations in the absence of N-hydroxyphthalimide (NHPI) as radical initiator. We propose that the activity of MIL-101 to generate benzyl radicals promoting autooxidation derives from the interaction of oxygen with the metal nodes of the lattice forming iron or chromium metalloperoxides with some radical character on the oxygen atom that will be able to abstract one hydrogen atom from the benzylic position. In support of our proposal it should be indicated that there are precedents in the literature describing for other metal complexes the formation of metal-superoxo species, M-$O_2^{\cdot -}$ of Cr(III) or Fe(III) as metals.[50-52] These species exhibit activity to perform C-H bond activation in hydrocarbons.[50,52] In addition, hemo groups containing Fe^{2+} are the natural O_2 carriers in blood and biological systems.[53-55] In the literature there are also some precedents using MIL-101(Cr) as catalyst for the benzylic oxidation of hydrocarbons, but always using TBHP as oxidizing reagent. Herein, we have shown that this oxidation can be promoted in the absence of TBHP. We previously showed that aerobic benzylic oxidation can also be carried out in the presence of various Cu-containing MOFs.[14,37] Scheme 2 summarizes our mechanistic proposal. Thus, this mechanistic proposal is, in a certain way similar to that previously proposed for NHPI/Fe(BTC) except that in this case the radical initiator will be spontaneously formed by interaction of the metal clusters with oxygen, a fact that was not observed for commercial Fe(BTC). The influence of activation for MIL-101(Fe) increasing its catalytic activity suggest that Fe(II) is more efficient than Fe(III) to form these metal peroxo species, although it could also be that removal of some water molecules acting as ligands of Fe(III) makes free positions around Fe(III) ions available for interaction with molecular oxygen.



Scheme 2. Mechanistic proposal for the aerobic oxidation of benzylic hydrocarbons using MIL-101(Cr) as catalyst.

Furthermore, selective $O_2^{\cdot -}$/HOO$^{\cdot}$ radical scavenging experiments were carried out using *p*-benzoquinone[56] and observing that the reaction is completely inhibited (Figure S22). This quenching studies support $O_2^{\cdot -}$/HOO$^{\cdot}$ radicals as the primary radical species promoting the autooxidation reaction. In other experiments, dimethylsulfoxide (DMSO) was employed as selective HO$^{\cdot}$ radical scavenger[57,58] and observing that the catalytic reaction is partially quenched (Figure S22). This experiment indicates the homolytic rupture of R-O-O-H species leading to the formation of R-O$^{\cdot}$ and HO$^{\cdot}$ radicals. Interestingly, the presence of DMSO resulted in an increase of selectivity to -ol/-one respect similar experiments in the absence of DMSO, suggesting that highly aggressive and reactive HO$^{\cdot}$ radicals contribute to the lack of selectivity in a large extent (Figure S22b).

CONCLUSIONS

Overall, the present data open new views on MOFs as oxidation catalysts showing that MIL-101 can generate carbon centred radicals in the presence of molecular oxygen and that adsorption within the internal pores can play a role improving product selectivity towards the wanted ol/one mixture as consequence of performing the oxidation in a confined reaction cavity. It should be commented that currently industrial processes based on aerobic oxidation like cyclohexane oxidation, are carried out at conversions below 5 % in order to obtain ol/one selectivities above 90 %, simplifying cumbersome mixture purification. In the area of aerobic oxidations a significant step forward would be to increase conversions without lowering selectivity below 90 %.

EXPERIMENTAL SECTION

Materials. All the reagents used in this work supplied by Sigma-Aldrich were of analytic grade. Except ethylbenzene that was distilled before use to remove radical quenchers, the other reagents were employed as received.

Catalyst preparation. MIL-101(Cr) was prepared following the procedure described by G.Ferey.[49] Briefly, terephthalic acid (0.25 g, 1.5 mmol) and $Cr(NO_3)_3 \cdot 9H_2O$ (0.4 g, 1 mmol) were added to a Teflon-lined autoclave containing 8 mL of demineralized water and 10 µl of HF. Then, the autoclave was heated at 200 ºC for 8 h. After cooling to room temperature, the resulting precipitate was washed with dimethylformamide (DMF) and ethanol and separated by filtration.

MIL-101(Fe) was synthesized following previously reported protocols. Typically, terephthalic acid (0.206 g, 1.25 mmol) and $FeCl_3 \cdot 6H_2O$ (0.675 g, 2.5 mmol) were added to a

Teflon-lined autoclave containing 15 mL of DMF. The autoclave was heated at 135 ºC for 8 h. After this time, the system was cooled to room temperature and the resulting precipitate was filtered and washed with ethanol.

Catalytic experiments. Typically, the required amount of catalyst (75 mg) was added to a round-bottom flask (25 mL). When necessary, the activation of MIL-101(Fe) or MIL-101(Cr) was carried out at 120 ºC under vacuum for 6 h. The reaction system was purged with molecular oxygen, air or argon using a balloon, the required amount of substrate introduced (i.e. 20 mmol) and the system sonicated for 15 min. Subsequently, the reaction mixture was placed in a preheated bath at 120 ºC and magnetically stirred.

Activation energy for cumene or 1,3-diisopropylbenzene was estimated by plotting the natural logarithm of the initial reaction rate of indane dissapearance versus the reciprocal of the absolute temperature and observing a linear correlation according the Arrhenius law.

Selective quenching experiments of $O_2^{\cdot -}$/HOO$^{\cdot}$ or HO$^{\cdot}$ radicals were carried out as described above, but in the presence of 20 mol % of *p*-benzoquinone or dimethylsulfoxide respect to the substrate. [56-58]

Adsorption experiments. To a round-bottom flask (25 mL) 1 mmol of a given substrate (indane, indanol or indanone) and *p*-xylene as solvent (3 mL) were added. Then, 75 mg of MIL-101(Cr) or MIL-101(Fe) were introduced and adsorption was allowed occurring at constant ambient temperature (21 °C). Aliquots of the mixture were analyzed at different times using a weighed amount of nitrobenzene as external standard to quantify the proportion of substrate remaining in the liquid phase. The maximum adsorbed amount for each substrate was determined in these assays and, then, molar ratios of indane/indanol or indane/indanone were calculated based on adsorption of a single compound. Similarly, isothermal competitive adsorption experiments were performed, but using mixtures of two substrates in proportions expected under reaction conditions, namely indane (1 mmol)/indanol (0.1 mmol) or indane (1 mmol)/indanone (0.1 mmol) and the maximum adsorbed molar ratios of indane/indanol and indane/indanone were determined. Also, isothermal adsorption experiments were performed by using a mixture of three compounds, namely indane (1 mmol), indanol (0.1 mmol) and indanone (0.1 mmol) in order to evaluate the maximum adsorbed molar ratio of indane/(indanol+indanone).

For the shape selectivity study, adsorption of cumene and 1,3-diisopropylbenzene was carried out. Cumene or 1,3-diisopropylbenzene (1 mmol) were dissolved in *p*-xylene (3 mL) and placed in a round-bottom flask. Then, MIL-101(Cr) (75 mg) was added and the suspension magnetically stirred. Analysis of different aliquots indicates that a fraction of the initial amount of cumene or 1,3-diisopropylbenzene was adsorbed in MIL-101(Cr) with the values of 0.077 mmol/75 mg and 0.033 mmol/75 mg, respectively, equivalent to 0.12 or 0.07 mg of aromatic compound/mg of MIL-101.

Product analysis. Aliquots of the reaction mixture at different times were diluted in a solution of toluene containing a known amount of nitrobenzene as external standard. Then, the samples were analyzed by gas chromatography (GC) using a flame ionization detector. In most cases, quantification was carried by using calibration curves of commercial samples and nitrobenzene as standard.

Leaching experiments. At the end of the reaction the catalyst was filtered through a 0.2 μm nylon filter. Then, the organic phase was put in contact with 30 mL of an HNO_3 aqueous solution (3 M) and the system heated at 80 ºC for 24 h. Finally, the presence of Cr or Fe in the aqueous phase was analyzed by chemical analysis using a ICP-AES instrument.

ASSOCIATED CONTENT

Supporting information includes time conversion plots for the aerobic oxidation of indane, ethylbenzene, *n*-butylbenzene, iso-butylbenzene, 1-bromo-4-butylbenzene, *sec*-butylbenzene, cumene and 1,3-diisopropylbenzene under different reaction conditions and isothermal adsorption measurements of indane, indanol or indanone on MIL-101 solids. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

* Corresponding author: hgarcia@qim.upv.es

Notes

The authors declare no competing finalcial interest.

ACKNOWLEDGMENTS

Financial support by the Spanish Ministry of Economy and Competitiveness (Severo Ochoa and CTQ2012-32315) is gratefully acknowledged. Generalidad Valenciana is also thanked for funding (Prometeo 2012/013 and GV/2013/040).

ABBREVIATIONS

MIL, Materieaux de l'Institute Lavosier; MOF, metal organic framework; TEMPO, 2,2,6,6-tetramethyl-1-piperidinyloxy; AIBN, azobisisobutyronitrile; TBHP, *tert*-butylhydroperoxyde; NHPI, N-hydroxyphthalimide; TON, turnover number; TOF, turnover frequency.

REFERENCES

(1) Corma, A.; Garcıia, H.; Llabrés i Xamena, F. X. *Chem. Rev.* **2010**, *110*, 4606-4655.

(2) Yoon, M., Srirambalaji, R., Kim, K. *Chem. Rev.* **2012**, *112*, 1196-1231.

(3) Furukawa, H., Cordova, K.E., O'Keeffe, M., Yaghi, O.M. *Science* **2013**, *341*, 1230444 (pages from 1 to 12).

(4) Dhakshinamoorthy, A.; Garcia, H. *Chem. Soc. Rev.* **2012**, *41*, 5262-5284.

(5) Dhakshinamoorthy, A., Opanasenko, M., Čejka, J., Garcia, H. *Catal. Sci. Technol.* **2013**, *3*, 2509-2540.

(6) Ranocchiari, M., Bokhoven, J.A.V. *Phys. Chem. Chem. Phys.* **2011**, *13*, 6388-6396.

(7) Wang, C., Zheng, M., Lin, W. *J. Phys. Chem. Lett.* **2011**, *2*, 1701-1709.

(8) Gu, Z.-Y., Park, J., Raiff, A., Wei, Z., Zhou, H.-C. *ChemCatChem* **2014**, *6*, 67-75.

(9) Gascon, J.; Corma, A.; Kapteijn, F.; Llabrés i Xamena, F. X. *ACS Catal.* **2014**, *4*, 361-378.

(10) Zalomaeva, O. V.; Chibiryaev, A. M.; Kovalenko, K. A.; Kholdeeva, O. A.; Balzhinimaev, B. S.; Fedin, V. P. *J. Catal.* **2013**, *298*, 179-185.

(11) Ivanchikova, I. D.; Lee, J. S.; Maksimchuk, N. V.; Shmakov, A. N.; Chesalov, Y. A.; Ayupov, A. B.; Hwang, Y. K.; Jun C.-H.; Chang, J.-S.; Kholdeeva, O. A. *Eur. J. Inorg. Chem.* **2014**, *1*, 132-139.

(12) Maksimchuk, N. V.; Kholdeeva, O. A.; Kovalenko, K. A.; Fedin, V. P. *Isr. J. Chem.* **2011**, *51*, 281-289.

(13) Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. *Catal. Sci. Technol.* **2011**, *1*, 856-867.

(14) Llabrés i Xamena, F. X.; Casanova, O.; Tailleur, R. G.; Garcia, H.; Corma, A. *J. Catal.* **2008**, *255*, 220-227.

(15) Luz, I.; León, A.; Boronat, M.; Llabrés i Xamena, F. X.; Corma, A. *Catal. Sci. Technol.* **2013**, *3*, 371-379.

(16) Kholdeeva, O. A. *Catal. Sci. Technol.* **2014**, *4*, 1869-1889.

(17) Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. *J. Catal.* **2012**, *289*, 259-265.

(18) Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. *ACS Catal.* **2011**, *1*, 48-53.

(19) Ishii, Y.; Sakaguchi, S. *Catal. Today* **2006**, *117*, 105-113.

(20) Iwahama, T.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1995**, *36*, 6923-6926.

(21) Iwahama, T.; Yoshino Y.; Keitoku T.; Sakaguchi, S.; Y., I. *J. Org. Chem.* **2000**, *65*, 6502-6507.

(22) Maksimchuk, N. V.; Kovalenko, K. A.; Fedin, V. P.; Kholdeeva, O. A. *Chem. Commun.* **2012**, *48*, 6812-6814.

(23) Brown, K.; Zolezzi, S.; Aguirre, P.; Venegas-Yazigi, D.; Paredes-García, V.; Baggio, R.; Novak, M.; Spodine, E. *Dalton Trans.* **2009**, *8*, 1422-1427.

(24) Kholdeeva, O. A.; Skobelev, I. Y.; Ivanchikova, I. D.; Kovalenko, K. A.; Fedin, V. P.; Sorokin, A. B. *Catal. Today* **2014**, *238*, 54-61.

(25) Maksimchuk, N. V.; Kovalenko, K. A.; Fedin, V. P.; Kholdeeva, O. A. *Adv. Synth. Catal.* **2010**, *352*, 2943-2948.

(26) Saedi, Z.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Mohammadpoor-Baltork, I. *Catal. Comm.* **2012**, *17*, 18-22.

(27) Qi, Y.; Luan, Y.; Yu, J.; Peng, X.; Wang, G. *Chem. Eur. J.* **2015**, 1589-1597.

(28) Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. *J. Catal.* **2009**, *267*, 1-4.

(29) Kim, J.; Bhattacharjee, S.; Jeong, K.-E.; Jeong, S.-Y.; Ahn, W. S. *Chem. Commun.* **2009**, 3904-3906.

(30) Ramos-Fernandez, E. V.; Garcia-Domingos, M.; Juan-Alcaniz, J.; Gascon, J.; Kapteijn, F. *Appl. Catal. A-Gen.* **2011**, *391*, 261-267.

(31) Song, G.-Q.; Lu, Y.-X.; Zhang, Q.; Wang, F.; Ma, X.-K.; Huang, X.-F.; Zhang, Z.-H. *RSC Adv.* **2014**, *4*, 30221-30224.

(32) Sun, J.; Yu, G.; Huo, Q.; Kan, Q.; Guan, J. *RSC Adv.* **2014**, *4*, 38048-38054.

(33) Hamidipour, L.; Farzaneh, F. *Reac. Kinet. Mech. Cat.* **2013**, *109*, 67-75.

(34) Skobelev, I. Y.; Kovalenko, K. A.; Fedin, V. P.; Sorokin, A. B.; Kholdeeva, O. A. *Kinet. Catal.* **2013**, *54*, 607-614.

(35) Skobelev, I. Y.; Sorokin, A. B.; Kovalenko, K. A.; Fedin, V. P.; Kholdeeva, O. A. *J. Catal.* **2013**, *298*, 61-69.

(36) Llabrés i Xamena, F. X.; Casanova, O.; Galiasso Tailleur, R.; Garcia, H.; Corma, A. *J. Catal.* **2008**, *255*, 220-227.

(37) Luz, I.; León, A.; Boronat, M.; Llabrés i Xamena, F. X.; Corma, A. *Catal. Sci. Technol.* **2013**, *3*, 371-379.

(38) Milas, N. A. *Chem. Rev.* **1932**, *10*, 295-364.

(39) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879-2932.

(40) Fares, M. M.; El-Khateeb, M.; Asali, K. J. *J. Inorg. Organomet. Polym.* **2003**, *13*, 143-155.

(41) Kharasch, M. S.; Fono, A.; Nudenberg, W. *J. Org. Chem.* **1951**, *16*, 105-112.

(42) Leclerc, H.; Vimont, A.; Lavalley, J. C.; Daturi, M.; Wiersum, A. D.; Llewellyn, P. L.; Horcajada, P.; Ferey, G.; Serre, C. *Phys. Chem. Chem. Phys.* **2011**, *13*, 11748-11756.

(43) Yoon, J. W.; Seo, Y.-K.; Hwang, Y. K.; Chang, J.-S.; Leclerc, H.; Wuttke, S.; Bazin, P.; Vimont, A.; Daturi, M.; Bloch, E.; Llewellyn, P. L.; Serre, C.; Horcajada, P.; Grenche, J.-M.; Rodrigues, A. E.; Férey, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 5949-5952.

(44) Vimont, A.; Thibault-Starzyk, F.; Datur, M. *Chem. Soc. Rev.* **2010**, *39*, 4928-4950.

(45) Devic, T.; Serre, C. *Chem.Soc.Rev.* **2014**, *43*, 6097-6115.

(46) Helm, L.; Merbach, A., E. *Chem. Rev.* **2005**, *105*, 1923-1959.

(47) Bruice, T. C. *Accounts of Chemical Research* **1991**, *24*, 243-249.

(48) Hansen, C. B.; Drenth, W. *Catalysis Letters* **1993**, *20*, 359-364.

(49) Ferey, G.; Mellot-Draznieks, C.; Serre, C.; Millange, F.; Dutour, J.; Surble, S.; Margiolaki, I. *Science* **2005**, *309*, 2040-2042.

(50) Ansari, A.; Jayapal, P.; Rajaraman, G. *Angew. Chem. Int. Ed.* **2015**, *54*, 564 -568.

(51) Cho, J.; Woo, J.; Nam, W. *J. Am. Chem. Soc.* **2010**, *132*, 5958-5959.

(52) Cho, K.-B.; Kang, H.; Woo, J.; Park, J. Y.; Seo, M. S.; Cho, J.; Nam, W. *Inorg. Chem.* **2014**, *53*, 645-652.

(53) Bocian, D. F.; Findsen, E. W.; Hofmann, J. A.; Schick, G. A.; English, D. R.; Hendrickson, D. N.; Suslick, K. S. *Inorg. Chem.* **1984**, *23*, 800-807.

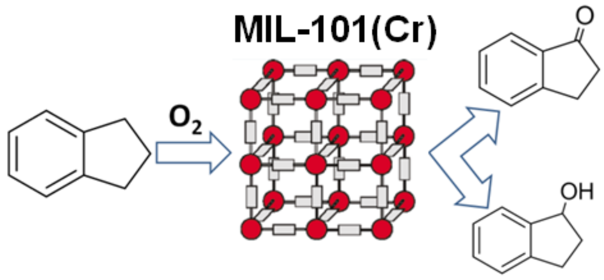
(54) Shumaev, K. B.; Gubkin, A. A.; Serezhenkov, V. A.; Lobysheva, I. I.; Kosmachevskaya, O. V.; Ruuge, E. K.; Lankin, V. Z.; Topunov, A. F.; Vanin, A. F. *Nitric Oxide* **2008**, *18*, 37-46.

(55) Silva, A. L.; de Almeida, L. F.; Marques, A. L.; Costa, H. R.; da Silva, A. B.; de Jesus Gomes Varela Jr., J. *J. Mol. Model.* **2014**, *20*, 2131 (pages from 1 to 10).

(56) Dhakshinamoorthy, A.; Navalon, S.; Alvaro, M.; Garcia, H. *ChemSusChem* **2012**, *5*, 46-64.

(57) Burkitt, M. J.; Mason, R. P. *Proc. Natl. Acad. Sci. USA* **1991**, *88*, 8440-8444.

(58) Martin, R.; Navalon, S.; Delgado, J. J.; Calvino, J. J.; Alvaro, M.; Garcia, H. *Chem. Eur. J.* **2011**, *17*, 9494-9502.



MIL-101(Cr) promotes the autooxidation of benzylic hydrocarbons with high selectivity