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ARTICLE

The effect of an electron-withdrawing group in the imidazolium cation: the case of nitro-functionalized imidazolium salts as acidic catalysts for the acetylation of glycerol

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The acetylation of glycerol was achieved with high conversion and selectivity towards triacetin at low temperatures and short reaction times by using acidic imidazolium salts as catalysts. Moreover, the addition of a nitro group to the imidazolium cation affords a much more competent catalyst, indicating a significant effect provided by the simple electronic change in the imidazolium cation. Theoretical calculations revealed increased polarization of the acidic hydrogen bond on the nitrated salts, which may be related to their superior catalytic behavior when compared to the non-functionalized salts. Combining the preliminary experimental and theoretical results, it is possible to suppose that the catalytic activity of acidic imidazolium salts may be better comprehended by its Brønsted acidities, but other parameters such as hardness, electronegativity, electrophilicity and ion-pair binding energy were also evaluated in order to investigate their effects in the acetylation of glycerol promoted by these acidic imidazolium salts.

Introduction

The global production of biodiesel has been steadily increasing in the past few years, coming along with the production of the process by-product glycerol. One of the options to deal with the increasing amounts of glycerol is adding value to glycerol by acetylation to produce triacetin, which can be used as an additive for biodiesel, gasoline, plastics and foods.[1, 2] Traditional methods for the industrial production of triacetin usually require long reaction times and high temperatures; therefore, catalysts must be used to achieve a less energy demanding process.

Many heterogeneous catalysts have been tested with promising results[1] for high glycerol conversion and easy separation from the products, but high costs and inactivation are common issues. Traditional homogeneous catalysts such as sulfuric acid and *p*-toluenesulfonic acid monohydrate ($TsOH.H_2O$), which can be used to achieve high conversion of glycerol at low cost, present a diversity of problems, such as corrosion of equipment, effluent contamination and recyclability of catalyst.[2] In this context, ionic liquids (ILs) have been used as alternative homogeneous catalysts that can be easily recycled without excessive deactivation after many runs,[3-5] since the structure of these compounds can be tailored to have increased catalytic activity under specific reaction conditions (task specific ionic liquids, TSILs). Therefore, it is expected that these TSILs can be used as catalysts for the production of triacetin in high conversions and selectivity at low temperatures, reaction times, cost and good recyclability. Several attempts to accomplish these goals have focused on increasing the number of Brønsted acidic sites in the ILs by adding sulfonic acid groups to the side chains of the cations or/and by using HSO_4^- as an anion, since the unmodified imidazolium cation is not significantly acidic.[6] This has been the main strategy for obtaining Brønsted acidic ILs since the early 2000s.[7] However, these modifications are expensive and synthetically slightly complicated.

In this work, we propose a simple and inexpensive approach to increase the natural acidity of the imidazolium cation by nitrating the imidazolium ring, which produces potentially more acidic protic imidazolium salts (the nitro-functionalized compounds are not technically ILs since their melting points are located above 100 °C, however, many of their properties are similar). The main goal here is to evaluate how the electronic change produced in the imidazolium ring by adding a nitro-functional group can influence the acidity/activity of the catalytic systems. We expect this new class of nitrated imidazolium salts to potentially increase the variety of simple and inexpensive Brønsted acidic compounds. The activity of five catalysts in the acetylation of glycerol (Scheme 1) were compared under similar conditions and the conversion of glycerol and selectivities towards different products were determined by ^{13}C-qNMR using a similar method as already described in the literature.[8] Computational studies were also conducted to determine the effect of the nitro group, as well as the change in anions, on a variety of molecular descriptors, which were correlated with the changes in catalytic activity. In order to have a broader understanding of these effects, additional calculations were performed for four ILs already described in the literature.[5]

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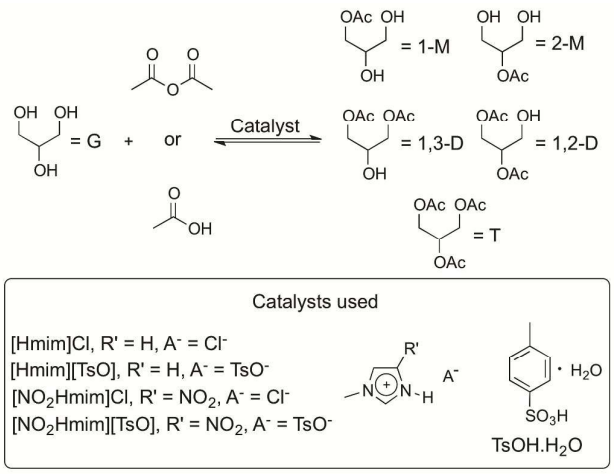

Scheme 1 Acetylation of glycerol with different acidic catalysts.

Results and discussion

Acetylation of glycerol

The acetylation of glycerol with acetic anhydride (AA) using no catalyst, at low temperatures (30 °C) and low reaction times (10 min), is negligible. This can be easily observed, since under these conditions, glycerol and AA form two phases, and the volume of glycerol remains apparently constant, indicating that occurs only a small amount of reaction. This low conversion has already been reported.[9] Full conversion of glycerol with high selectivity towards triacetin can be achieved without catalyst at high temperatures (120 °C) and long reaction times (120 min).[10] In reactions with acetic acid (AcOH) at high temperatures (110 °C) and low reaction times (20 min), conversion of 40% and negligible selectivity towards triacetin has been reported;[11] therefore, the conversion and selectivity would be even lower at lower temperatures. We were not able to quantify these blank reactions with our method, since it requires samples from a homogeneous reaction mixture in order to provide an accurate representation of the concentration of the different compounds in the mixture. In Table 1, we summarize the conversion and selectivity for the glycerol acetylation using the different catalysts. By comparing the activities of the catalysts, we observed that the nitro group added to the C5 position of the imidazolium cation increases considerably the activity of the imidazolium salts for acetylation. Moreover, the tosylate anion also positively affects the activity of the catalyst (Table 1). Indeed, the best results among the imidazolium salts were achieved for the salt [NO_2Hmim][TsO] (entry 19, Table 1), which can be used in a 1 mol% relation to glycerol to achieve 100% conversion to triacetin at 30 °C within 10 minutes using AA (molar ratio of 1:4 with glycerol). In addition, 94% of conversion of glycerol in acetins was also achieved using AcOH (ratio of 1:8) at 120 °C for 10 minutes with 1 mol% of catalyst (entry 18, Table 1). Conversions as high as 98% and selectivities of 29% to triacetin can be achieved using AcOH under different conditions (entry 16, Table 1).

Table 1 Acetylation of glycerol under different conditions[a]

Entry	Catalyst	Mass of Catalyst (g)	T (°C)	Time (min)	Acetylating agent	Glycerol:acetylating agent	Conversion (%)	Selectivity (%)				
								1-M	2-M	1,2-D	1,3-D	T
1	$TsOH.H_2O$	0.0953	60	10	AA	1:4	100	0	0	0	0	100
2[b]	$TsOH.H_2O$	0.0953	60	10	AcOH	1:8	89	51	6	11	29	3
3[b]	$TsOH.H_2O$	0.0953	120	10	AcOH	1:8	98	18	2	16	37	27
4	$TsOH.H_2O$	0.0100[c]	60	10	AA	1:4	100	0	0	0	0	100
5[b]	$TsOH.H_2O$	0.0100[c]	120	10	AcOH	1:8	97	30	4	17	39	10
6[b]	[Hmim]Cl	0.1500	60	10	AA	1:4	76	56	5	9	24	6
7	[Hmim]Cl	0.1500	60	10	AcOH	1:8	0	0	0	0	0	0
8[b]	[Hmim][TsO]	0.1500	60	10	AA	1:4	100	0	0	3	24	73
9	[Hmim][TsO]	0.1500	60	10	AcOH	1:8	0	0	0	0	0	0
10[b]	[NO_2Hmim]Cl	0.1500	60	10	AA	1:4	100	0	0	3	20	77
11	[NO_2Hmim]Cl	0.1500	60	10	AcOH	1:8	0	0	0	0	0	0
12	[NO_2Hmim][TsO]	0.1500	60	10	AA	1:4	100	0	0	0	0	100
13[b]	[NO_2Hmim][TsO]	0.1500	60	10	AcOH	1:8	61	76	9	3	13	0
14	[NO_2Hmim][TsO]	0.1500	30	10	AA	1:4	100	0	0	0	0	100
15	[NO_2Hmim][TsO]	0.1500	120	10	AcOH	1:8	98	19	2	17	36	26
16	[NO_2Hmim][TsO]	0.1500	120	120	AcOH	1:8	98	16	3	16	35	29
17	[NO_2Hmim][TsO]	0.0158[c]	120	10	AcOH	1:8	92	46	5	15	30	4
18[b]	[NO_2Hmim][TsO]	0.0158[c]	120	10	AcOH	1:8	94	40	8	14	33	5
19	[NO_2Hmim][TsO]	0.0158[c]	30	10	AA	1:4	100	0	0	0	0	100
20	[NO_2Hmim][TsO]	0.0158[c]	60	10	AA	1:4	100	0	0	0	0	100

[a] Conversion and selectivities determined by ^{13}C-qNMR; [b] 10 to 15 minutes of vacuum at 70 °C to eliminate the acetylating agent; [c] 1% mol catalyst/mol glycerol.

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Noteworthy, in cases without high conversions and selectivities towards triacetin, most of the acetylating agent was separated from the final reaction mixture using a Kugelrohr distillation apparatus in order to prevent the acetylation of glycerol and acetins inside the NMR tube. Entries 17 and 18 show that the distillation of the acetylating agent at the end of the reaction may have a small effect on the selectivities, but we do not consider that to be of great relevance. Another consideration is that equal mass amounts of catalysts were used because these compounds may serve as solvents as well as catalysts, so we attempted to compare them under similar conditions. Evidently, it would be more desirable to compare them in equal molar amounts as well, even though it is quite clear that there is a considerable difference in activities. Analyzing the entries 6, 8, 10 and 12 in Table 1 we noticed that by changing the Cl anion by the tosylate anion the conversion of glycerol and the selectivities towards triacetin increased significantly. The effect of the nitro group can be seen clearly when comparing entries 7, 9, 11 and 13. Moreover, it is worth to note that the catalyst [NO_2Hmim][TsO] is present in the smallest molar concentration when compared to the others, but it is still the most active.

To be able to comprehend the capabilities of [NO_2Hmim][TsO], the activity of this imidazolium salt was compared with a very common and effective acid catalyst, TsOH.H_2O. Surprisingly, the results observed in entries 1 and 12 (Table 1) show that TsOH.H_2O and [NO_2Hmim][TsO] provide the same conversion and selectivities when AA was used as acetylating agent. In the case of AcOH, entries 2 and 13 show that [NO_2Hmim][TsO] is not as active as TsOH.H_2O under these conditions, but the preferred selectivity for the mono-acetylated compound for the reaction in the imidazolium salt is also an interesting result. To demonstrate the true potential of our class of nitro-functionalized imidazolium salts, we started decreasing the reaction temperatures and the catalyst amounts. In fact, the reaction using AA in the presence of a minor amount of catalyst yields total conversion and selectivity to triacetin even at 30 °C within 10 minutes (entry 19, Table 1). However, to achieve high conversion with AcOH, higher reaction temperatures are required; therefore, entries 15 and 16 show that increasing the temperature to 120 °C can increase the conversion of glycerol drastically, whereas increasing the reaction time does not have the same effect. These results indicate that the reaction approaches equilibrium in very short times, close to 10 minutes. Decreasing the amount of the catalyst to 1 mol% in relation to glycerol produces a significant decrease in selectivity towards triacetin, but the conversion of glycerol continues excellent and the 1-M product was formed preferably (entry 17, Table 1). If we compare this result with entry 3, it is possible to note that [NO_2Hmim][TsO] has a remarkable activity, approaching the one observed for the TsOH.H_2O catalyst. This can be considered as an outstanding result, taking into consideration the comparison of an imidazolium salt with a strong organic acid. In comparison to a previous work,[6] our results evidenced the considerable effect provided by the nitro group in the imidazolium cation. Indeed, the acetylation of AcOH using the salt [NO_2Hmim][TsO] afforded much superior conversions than an analogous protic imidazolium salt [Hmim][HSO_4] and similar to a double SO_3H-functionalized IL [$(HSO_3$-p$)_2$im][HSO_4], which is one of the most active systems based on acidic ILs reported to date. Therefore, we propose that a simple change in the electronic properties of the imidazolium cation by adding an electron-withdrawing group produces comparable results to those systems using several Brønsted acidic groups attached to the structure of imidazolium salts. These results indicate that simply increasing the number of Brønsted acidic sites is not necessarily the only option to increase the activity of imidazolium salts.

Computational studies

Our preliminary evaluation suggests that the increased activity of the nitro-functionalized imidazolium salt might be attributed to the electronic effect of the nitro group on the N-H bond of the imidazolium ring, increasing the acidity of the cationic species. In order to evaluate this effect, theoretical calculations were performed comparing the molecular descriptors of the non-functionalized and functionalized imidazolium salts. Conceptual Density Functional Theory reactional descriptors were calculated at the B3LYP-D3 and TPSS-D3 levels of theory using the basis sets 6-31+G* and 6-311++G(3df,3dp), respectively. The same calculations were performed using four ILs already described in the literature[5] in order to verify if the same hypothesis formulated to explain the activity of these protic imidazolium salts can be used to explain the behavior of more commonly used sulfonic acid functionalized ILs.

Electronic effect of the nitro group. As stated before, the electron withdrawing effect of the nitro group is likely the main responsible for increasing the acidity, and therefore the catalytic activity of the nitrated salts. This can be confirmed when comparing the maps of the molecular electrostatic potential of [Hmim][TsO] and [NO_2Hmim][TsO] (Fig. 1).

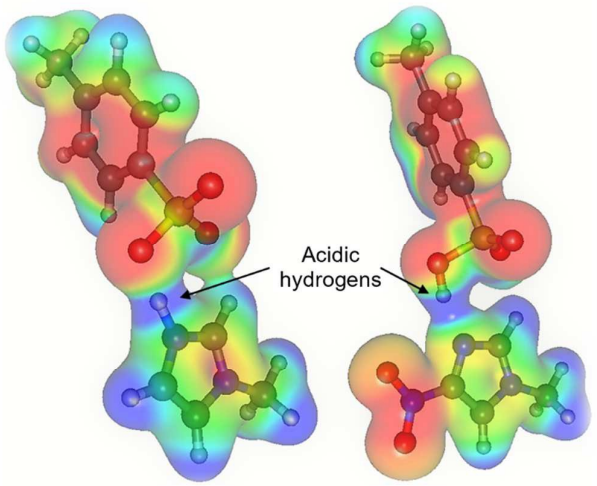

Fig. 1 Molecular electrostatic potential maps at the B3LYP-D3/6-31+G* level of theory for [Hmim][TsO] (left) and [NO_2Hmim][TsO] (right). Red color: negative potential; blue color: positive potential. Isosurface value of 0.016803 and grid from -0.09 to 0.09.

It is clear that the nitro group increases the charge polarization around the acidic hydrogen, which may increase its acidity. This polarization is evident due the presence of two electron withdrawing regions in the molecule, the SO_3 group on the anion and the NO_2 group on the cation. This effect appears to be quite strong, since at the B3LYP-D3/6-31+G* level of theory the acidic hydrogen is transferred to the SO_3 group of the tosylate anion. Similar results have been found for the [NO_2Hmim]Cl. For a non-nitrated salt, this effect was only observed in the case of [Hmim]Cl at the TPSS-D3/6-311++G(3df,3dp) level of theory. For all other non-nitrated salts, in both levels of theory, including the sulfonic acid functionalized ILs, this effect was not observed. This indicates that the acidic hydrogen in the nitrated salts is more weakly bonded

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to the cation, which means that it is more available to be transferred to another species, acting as a more effective acid catalyst when compared to non-nitrated salts.

Bond lengths and charges. The effect of the nitro group on the acidity can also be observed in the bond lengths of the acidic hydrogens and the charge densities around the acid group. We expected to find a correlation between increased bond lengths of the acidic hydrogens and the increased activity of the catalysts. This increase in bond length could indicate that these bonds are becoming weaker, which relates to more acidic hydrogens when compared with those exhibiting shorter bond lengths. And as can be observed in other works in the literature,[3, 6, 12] catalysts with high Brønsted acidity (characterized by their low values of Hammett acidity (H_0)) are usually more active and capable of achieving higher selectivities of triacetin.

Doubtless, these bond lengths can only be compared between similar compounds, since we should not expect to observe this correlation between Brønsted acidity and acidic hydrogen bond length in compounds that have completely different acidic groups. In the case of different acid groups, the differences in catalytic activity cannot be explained by using only bond lengths as an indication of acidity.

By analyzing the bond lengths of the acidic hydrogens (N-H bond and Anion-H bond) of our catalysts (Fig. 2), it is clear that the change in anion and the addition of the nitro group drastically influence the bond lengths. First, by comparing the lengths in the non-nitrated compounds we can observe that the N-H bond shrinks (from 1.21 to 1.10 Å) with the substitution of the chloride by the tosylate anion, which would indicate lower acidity. However, with the tosylate anion, the hydrogen is much more closely bonded to the anion than in the case of the chloride anion, so that effect of getting closer to the anion may positively affect its acidity. Other effects that will be discussed later can also account for this difference in activity, since bond lengths cannot be used as a single indicative of activity and acidity.

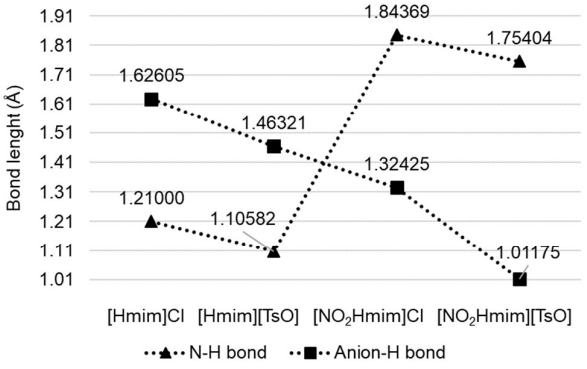

Fig. 2 Bond lengths for the different imidazolium salts calculated in the B3LYP-D3/6-31+G* level of theory. Increasing order of activity from the left to the right.

The electron withdrawing effect of the nitro group is very drastic, since the acidic hydrogen is transferred from the cation to the anion, as it can be observed in Fig. 1. This explains the lengthening of the N-H bond when comparing nitrated to non-nitrated salts (from 1.21 in [Hmim]Cl to 1.84 Å in [NO_2Hmim]Cl). One way of looking at this phenomenon, is that by nitrating these salts, the hydrogen becomes so weakly bonded to the imidazolium ring that it is behaving more likely the free hydrochloric acid or tosylic acid, and not as a salt. Therefore, we can hypothesize that the farther away the hydrogen is from the cation, and the closer it is to the anion, the more acidic it may be, and then more catalytically active in the context of acid catalysis. Since our sample of compounds is too small (only four imidazolium salts), we thought that it would be interesting to apply our hypothesis in a different set of catalysts. Hence, we decided to perform all calculations for the present imidazolium salts and other four ILs previously reported in literature (Fig. 3), which were used for the same task under similar conditions.[5]

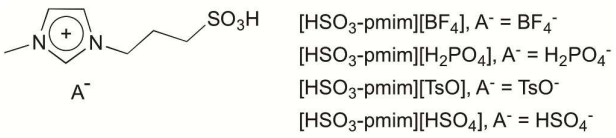

Fig. 3 Sulfonic acid-functionalized ILs reported in literature.[5]

These ILs were used as acidic catalysts for the acetylation of glycerol at different conditions (80-120 °C, 6 h, 1:8 glycerol:acetic acid molar ratio, ~14% mol catalyst in relation to glycerol and 10 mL of cyclohexane).[5] The reported results indicated that the ILs containing the anions HSO_4^- and TsO^- exhibited better activities at 80 °C and 120 °C, respectively, whereas BF_4^- had the worst performance followed by $H_2PO_4^-$ at 80 and 120 °C. Even though the conditions were different, we believe that the same hypothesis used to explain the behavior of our catalysts can be applied to these compounds and possibly many others, since their activity seems to be correlated to their acidity. A similar trend found in Fig. 2 regarding the lengthening of the O-H (N-H in the case of Fig. 2) bond and shortening of the anion-H bond can be observed in Fig. 4. The intensity of the changes in bond lengths from one IL to the other is considerably smaller than the ones in Fig. 2, since the only change in the structure is the anion, which does not have such a strong effect as the change in the structure of the cation.

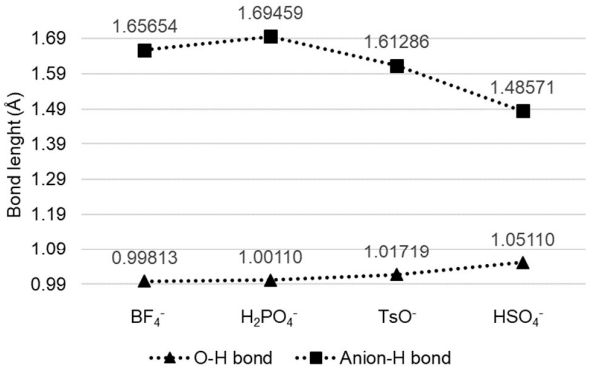

Fig. 4 Bond lengths for the reported ILs calculated in the B3LYP-D3/6-31+G* level of theory. Increasing order of activity from the left to the right.

Atomic charges. Atomic charges derived from the molecular electrostatic potential, such as CHELPG charges,[13] are numerical descriptions for the changes observed in the potential maps in Fig. 1. These charges can be easily calculated, at low computational cost, and are generally accepted as being more reliable than the

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conventional Mulliken charges for these compounds.[14] Our expectation is that the increase in the polarization of charges around the acidic hydrogen can increase its acidity and, consequently, its catalytic activity, since more polarized bonds are likely more acidic. Observing these atomic charges in Fig. 5, we can verify that [Hmim]Cl has the smallest charge in the acidic hydrogen and the biggest charge in the N atom; therefore, its Δ between charges (difference in absolute values between the charges in the acidic hydrogen and the nitrogen to which it is bonded) is the smallest (0.199). This Δ value increases with the substitution of the chloride by the tosylate anion, and increases even more when adding the nitro group to the cation.

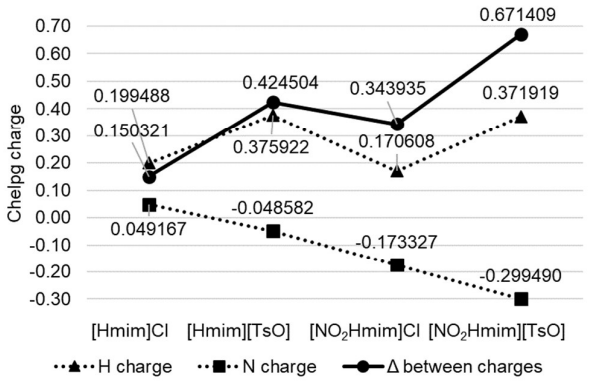

Fig. 5 CHELPG charges (in units of e) for the different salts calculated in the B3LYP-D3/6-31+G* level of theory.

This trend of increasing the Δ between charges is even larger if we consider the effect of transference of hydrogen (N-H group) from the nitrated cations to the anions. Since the acidic hydrogens are more closely bonded to the anions in the nitrated compound, it is possible to calculate the Δ values using the charges in the Cl and O (from the SO_3 group in the tosylate). The values of Δ varies from 0.34 to 0.49 for $[NO_2Hmim]Cl$ and from 0.67 to 0.91 for $[NO_2Hmim][TsO]$. Therefore, this transference of hydrogen caused by the NO_2 group increases even more the polarization of the bond on the acidic hydrogen.

Fig. 6 depicts the same trend of increased charge polarization observed in the previous reported SO_3H-functionalized ILs from Fig. 3. The anions appear to have an effect in the charges of the acidic group SO_3H in the cation, although, it is not as accentuated as the change in polarization induced by the nitro group.

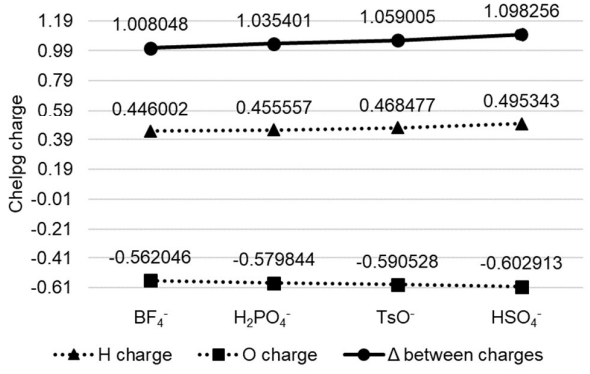

Fig. 6 CHELPG charges (in units of e) for the reported ILs calculated in the B3LYP-D3/6-31+G* level of theory.

The effect that the anion exerts on the polarization of the O-H bond becomes apparent when visualizing the molecular structure of these ILs. In all cases, the anions are interacting closely with the SO_3H and the C2-H bond, which are sites with high positive charges (Fig. 7). The anion appears to be polarizing the O-H bond, in a similar manner to the nitro group on $[NO_2Hmim][TsO]$, slightly pulling electronic density away from the acidic hydrogen. All anions have this effect to some extent, but HSO_4^- and TsO^- appear to have the strongest effect (largest value for Δ between charges).

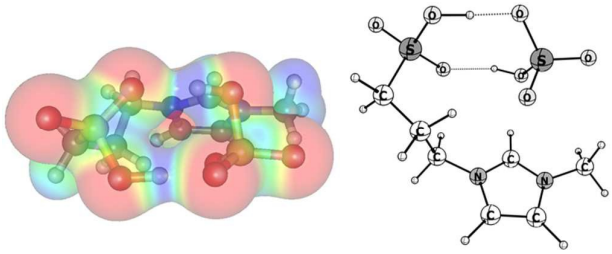

Fig. 7 Top perspective of the molecular electrostatic potential map for $[HSO_3pmim][HSO_4]$ (left) and its structure (right). Red color: negative potential; blue color: positive potential. Isosurface value of 0.016803 and grid from -0.09 to 0.09.

Evaluation of electronic descriptors. One may ask if in fact the Brønsted acidity is the only property to be considered in these cases. The well-known classical mechanism for acetylation reactions involves an initial proton transfer from the catalyst to the substrate and subsequent nucleophilic attack of the substrate by glycerol. Doubtless, the proton transfer path is fundamental for the occurrence of the reaction, but if the pK_a value is the only important aspect, it would be expected that the reactions employing strong acids (H_2SO_4,[6] TsOH, this work) should exhibit much better results than the nitro-imidazolium salts. In this context, we have tried to explore additional explanations for the observed catalytic activity of the nitro-functionalized imidazolium salts, which include the concepts of Lewis and Pearson. Analyzing the energy differences between the frontiers orbitals (HOMO and LUMO) of the involved species, it is possible to define important properties, such as hardness (η), electronegativity (χ) and electrophilicity (ω); the first two can be used to determine electron flow tendencies (ΔN)[15-17] between the reactive species. Single point energies can also be used to calculate ion-pair binding energies (IPBE), which can quantify the strength of the interactions between cation and anion.[18]

Hardness, electronegativity and electrophilicity. According to Pearson,[15] compounds with a large energy gap between HOMO/LUMO orbitals are hard, whereas those with a small energy gap are soft. Observing the HOMO/LUMO gap values and the hardness of the compounds (Table 2), it is probable that hard-hard interactions prevail in these cases. Therefore, this is a case of charge-controlled reactions.[19] This may be the reason why these kind of reactions are so well explained by charge distribution, in contrast to soft-soft reactions that need to be analyzed using frontier orbital densities. This may be an important factor if one plans to use these kind of catalysts for other applications, since they may not perform as well as expected for reactions involving soft compounds. In our study, we could not find convincing evidence

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that small changes in hardness impact the overall performance of the catalysts, a broader sample of catalysts would be necessary to ascertain the importance of hardness values.

Table 2 Molecular descriptors for all compounds discussed in this work. Calculated at B3LYP-D3/6-31+G* level of theory

Compound	Electronegativity χ (eV)	Electrophilicity ω (eV)	Hardness η (eV)
Glycerol	3.78945	1.9836	3.6197
Acetic acid	4.01805	2.0994	3.8451
Acetic anhydride	4.4637	2.9712	3.3530
p-TSA	4.4769	3.3581	2.9842
[Hmim]Cl	3.52505	2.5981	2.3914
[Hmim][TsO]	3.63325	2.6093	2.5296
[NO_2Hmim]Cl	5.3437	5.6502	2.5269
[NO_2Hmim][TsO]	4.92005	5.4647	2.2149
[HSO_3-pmim][BF_4]	4.983	3.9105	3.1748
[HSO_3-pmim][H_2PO_4]	4.2858	3.3098	2.7748
[HSO_3-pmim][TsO]	4.1124	3.3227	2.5449
[HSO_3-pmim][HSO_4]	4.31345	3.3392	2.7860

At this point, we cannot discard the possibility that Lewis acidity plays a role in the mechanism of acetylation of glycerol. For this reason, we will also explore concepts regarding the Lewis acidity of these compounds presented in Table 2. For compounds to behave like Lewis acids, they need higher values of electronegativity when compared to the bases they are reacting with.[15] The bases in this case are acetic acid and acetic anhydride, since they will transfer electrons to the salts in order to initiate the catalytic cycle of glycerol acetylation. By this assumption, [Hmim]Cl and [Hmim][TsO] should have low catalytic activity, since their electronegativity is lower than acetic acid and acetic anhydride. On the other hand, [NO_2Hmim]Cl and [NO_2Hmim][TsO] are predicted to act as acids, since their electronegativity is higher than acetic acid and acetic anhydride. This estimative is well supported by our experimental evidences, as showed in Table 1.

Considering the already reported SO_3H-functionalized ILs (Fig. 3), we can confirm that all of them should behave as acids when reacting with AcOH, but this trend could change in a reaction with AA, since the only catalyst with electronegativity higher than it, is [HSO_3-pmim][BF_4]. Then, it is reasonable to suppose that the Lewis acidity of the compounds is not involved in the reaction mechanism, only their Brønsted acidity.

Electrophilicity can be considered as a thermodynamical descriptor related to the strength of the Lewis acidic character of a molecule, where higher values indicate a stronger Lewis acid.[17] It should not be confused with experimental measures of electrophilicity, since those are kinetic measurements. It is not clear whether small changes in the value of this descriptor are relevant in the acetylation of glycerol, since they do not correlate with activity, but larger changes, such as those from the non-nitrated salts [Hmim]Cl and [Hmim][TsO] to the nitrated ones, may be relevant (changes of more than 1-1.5 eV). At this point, we cannot confirm if the increase in electrophilicity is responsible for the increase in activity because more data points would be required to evaluate the role of Lewis acidity in the mechanism of this acid catalysis.

Electronic flow between reactive species. Another information that the descriptors from Table 2 can provide are the ΔN values between reactive species. These ΔN values are derived from electronegativity and hardness of both acids and bases reacting, in our case, the catalysts act as acids and the acetylating agents act as bases. The traditional Fischer esterification mechanism involves the transference of hydrogen from the acid catalyst to the carbonyl group on the acetylating agent in order to increase the electrophilicity of the carbon on the carbonyl group, making it easier for the glycerol to perform a nucleophilic attack. We can also analyze this mechanism using the Lewis acidity model. By this point of view, there is an electron transfer from the oxygen of the carbonyl of the acetylating agent to the catalyst. As we stated before, in order to have electronic flow from the acetylating agent to the catalyst, the catalysts need higher electronegativity values when compared to the acetylating agent. ΔN values (Table 3) can provide information about the direction of the electronic flow and the scale of the transference.

Table 3 Electronic flow tendencies (in units of e) for all catalysts discussed in this work. Calculated at B3LYP-D3/6-31+G* level of theory

Compound	ΔN from AcOH	ΔN from AA
p-TSA	0.0336	0.0010
[Hmim]Cl	-0.0395	-0.0817
[Hmim][TsO]	-0.0302	-0.0706
[NO_2Hmim]Cl	0.1040	0.0748
[NO_2Hmim][TsO]	0.0744	0.0410
[HSO_3-pmim][BF_4]	0.0687	0.0398
[HSO_3-pmim][H_2PO_4]	0.0202	-0.0145
[HSO_3-pmim][TsO]	0.0074	-0.0298
[HSO_3-pmim][HSO_4]	0.0223	-0.0122

As it was discussed before, since we are dealing with hard-hard interactions, the flow of electron is very limited, varying from 0.001 to 0.10 electrons. The most interesting observation we made is that the non-nitrated salts [Hmim]Cl and [Hmim][TsO] have negative values for both ΔN (from AcOH and AA), which indicates that the electronic flow tendencies are reversed. Hence, they are acting like Lewis bases, and not like acids. The nitro-functionalized imidazolium salts act like acids when reacting with AcOH and AA, whereas the negative ΔN values from AA observed for the reported SO_3H-functionalized ILs [HSO_3-pmim][H_2PO_4], [HSO_3-pmim][TsO] and [HSO_3-pmim][HSO_4] suggest a lower activity in the reaction with AA when compared to [HSO_3-pmim][BF_4]. Notably, it is difficult to define how significant are these Lewis and Pearson acidities in

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relation to the more broadly accepted Brønsted acidity in these acid reactions.

Ion pairing effects. The effect that the strength of interactions between anion and cation of the imidazolium salts could have on the catalyst activity is another aspect to be considered. In this context, the ion-pair binding energies (IPBE) were calculated (Table 4). Low values indicate stronger interaction between the ions and high values indicate weaker interactions. It is expected that ionic pairs with strong interaction may trap the acidic hydrogens, decreasing the Brønsted acidity of the salt. Therefore, high IPBE values should be related to a superior acid activity. Comparing [Hmim]Cl with [Hmim][TsO] it is apparent that the chloride anion is more strongly bound to the anion, and this effect may reduce the acidity of the chloride salts. This appears to be the case for nitrated salts ([NO_2Hmim]Cl and [NO_2Hmim][TsO]) as well. The nitro group also appears to have an effect on the IPBE; it increases the interaction between anions, resulting in a lower IPBE when compared to the non-nitrated salts. This indicates that the nitro group should decrease the acidity of these compounds, but the inverse is observed due to more relevant electronic effects. Consequently, these results demonstrate the importance of not analysing IPBE isolated from other descriptors in an attempt to explain the acidity of these compounds. This descriptor, as most others, needs to be considered in conjunction with other descriptors to accurately characterize the acidity of these compounds.

For the known SO_3H-functionalized ILs, we should expect that the IL [HSO_3-pmim][TsO] would be much more active than [HSO_3-pmim][HSO_4], since there is a considerable difference in IPBE between the two compounds. However, the IL [HSO_3-pmim][TsO] is the slightly more active catalyst above 120 °C (only 2% more selectivity towards triacetin). Hence, the IPBE does not appear to be capable of accounting for the differences in activity between the SO_3H-functionalized ILs. Although the coordination properties of the anions in the 3D structural organization of the imidazolium salt are important aspects to be considered, the use of the IPBE concept isolated from other descriptors may not be accurate to the reality of these ionic compounds (the ions can easily separate in solution), which makes the hypothesis that acidic hydrogens can be trapped due to strong ionic interactions less likely. Therefore, more studies need to be conducted to determine if there is a correlation between IPBE and acidity. Moreover, other possible effect of the tosylate anion, in contrast to the chloride, may be the stabilization of the transition states by π-π stacking interaction with the imidazolium cation.

Table 4 Ion-pair binding energies (IPBE). Calculated at TPSS-D3/6-311++G(3df,3dp) level of theory and counterpoise corrected

Compound	IPBE (kcal/mol)
[Hmim]Cl	-43.4852
[Hmim][TsO]	44.1177
[NO_2Hmim]Cl	-55.0230
[NO_2Hmim][TsO]	33.5756
[HSO_3-pmim][BF_4]	45.1772
[HSO_3-pmim][H_2PO_4]	44.0702
[HSO_3-pmim][TsO]	110.0844
[HSO_3-pmim][HSO_4]	43.7090

The intention with these particular theoretical studies is to highlight the possible existence of other acid-base aspects in the acetylation of glycerol promoted by imidazolium salts. Possibly the argument that imidazolium salts are acting as simple proton donator is the preferable manner to explain the activities in acidic reactions, but the influence of other parameters may be investigated in order to help the understanding of the catalytic behavior of these 3D supramolecular organized compounds.

Conclusions

In summary, we have demonstrated the use of nitro-functionalized imidazolium salts as efficient catalysts for the acetylation of glycerol under relatively mild conditions. The results demonstrate that the introduction of an electron-withdrawing group in the imidazolium cation affects the acidity/activity of the salt, which is sufficient to provide excellent performances for the acetylation of glycerol. Indeed, high conversions and selectivities were obtained in the reaction employing AA or AcOH, approaching the results obtained by a classical strong organic acid, TsOH.H_2O. Moreover, the reaction could be carried out without the use of solvents, such as toluene typically used for the azeotropic distillation of water. Our system is a new approach to increase the Brønsted acidity of this class of imidazolium salts, where the electronic properties can be tuned by the simple inclusion of a functional group in the imidazolium ring. The present method seems to be very promising due to the preparation of a simpler and cheaper catalyst, when compared to more sophisticated and expensive SO_3H-based ILs. Notably, the claim of this study is not to make a direct comparison of the properties and activities of the nitro-functionalized imidazolium salts with other acidic catalysts already described in the literature, but open possibilities for the creation of new and improved acidic imidazolium compounds that are not based on the usual SO_3H functionalization, but instead, rely on increasing the natural acidity of the N-H group. It is preferable that the Brønsted acidity is the main factor to be considered in the development of these kind of acidic catalysts, but more studies need to be conducted in order to confirm the influence of other parameters such as hardness, electrophilicity and electronegativity in the acid activity of imidazolium salts. In fact, we have confidence that this work will serve as a starting point to a more comprehensive study of the properties that govern the activity of these imidazolium compounds. We also expect that these findings can be useful for the design of new acidic imidazolium salts/ionic liquids with specific structural features for several acid-promoted applications.

Experimental

General information

All reagents were purchased from various commercial suppliers and were used without further purification, with the exception of 1-methylimidazole that was purified by distillation. All ^{1}H and ^{13}C NMR spectra were acquired using a Varian MR-400 (400 MHz and 101 MHz, respectively), with the exception of the 1-methyl-4-nitroimidazole spectra, which were acquired with a Bruker Avance

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III HD 400 MHz (HMBC) and a Bruker Ascend 400 MHz (HSQC). All FTIR spectra were acquired using a Bruker Alpha with a Platinum ATR module. Melting points were acquired using a Buchi B-540 with sealed capillary glass tubes.

Synthesis of compounds

4(5)-nitroimidazole. This method was based on a previously published work.[20] Nitric acid (86 mL, 68%, 0.93 mol) was added dropwise to imidazole (10 g, 0.15 mol) in a round-bottom flask with a magnetic stir bar over an ice bath. After adding all the nitric acid, the solution was stirred for a couple of minutes until it cooled down to the ice bath temperature. Then, sulfuric acid (41 mL, 98%, 0.41 mol) was added in the same way as the nitric acid, the solution was then stirred over an ice bath for 30 min. The reaction mixture was then refluxed overnight and then allowed to cool down to room temperature. The reaction mixture was submitted to an ultrasonic bath and compressed air was bubbled through it to decrease the amount of nitrogen oxides in solution, which gives it an orange color. The reaction mixture was then cooled down in the fridge and roughly 150 g of crushed ice was added to the solution. The white precipitate formed was filtered and washed with distilled water and dried under vacuum at 60 °C to obtain off-white crystals of 4(5)-nitroimidazole. δ_H (400 MHz, DMSO-d_6) 13.23 (1 H, br s, NH), 8.31 (1 H, s, CH), 7.84 (1 H, s, CH). δ_C (101 MHz, DMSO-d_6): 147.6 (C4-NO_2), 135.9 (C2), 119.1 (C5).

1-Methyl-4-nitroimidazole. This method was based on a previously published paper.[21] 4(5)-Nitroimidazole (10 g, 88.4 mmol) and potassium carbonate (18.35 g, 0.13 mol) were dispersed in 150 mL of acetonitrile. Iodomethane (6.6 mL, 106 mmol) dissolved in 50 mL of acetonitrile was added dropwise to the reaction mixture with magnetic stirring over an ice bath. After all the iodomethane solution was added, the solution was stirred for 30 min over an ice bath. The reaction mixture was then heated to 65 °C overnight. An Allihn type condenser attached to a cooling system was used to avoid solvent and reactant losses. The reaction mixture was filtered and the solid was washed with a small amount of acetonitrile and discarded. The acetonitrile from this washing was added to the rest of the reaction mixture. All the acetonitrile was then removed under vacuum using a rotary evaporator, the product was extracted from the solid reaction mixture using a mixture of dichloromethane and methanol (95:5 v/v). The solvents were removed under vacuum using a rotary evaporator. The slightly yellow solid that remained was recrystallized from 2-propanol. The product was an off-white solid. δ_H (400 MHz, DMSO-d_6): 8.35 (1 H, s, C5-H), 7.80 (1 H, s, C2-H), 3.76 (3 H, s, Me). δ_C (101 MHz, DMSO-d_6): 146.9 (C4-NO_2), 138.1 (C2), 122.6 (C5), 34.2 (Me). HMBC and HSQC analyses are shown in the SI (Fig. S1 and S2, respectively).

General procedure for the synthesis of the imidazolium salts. In a Schlenk flask with a magnetic stir bar over an ice bath were dissolved or dispersed imidazole compounds (4(5)-Nitroimidazole, 1-Methylimidazole or Imidazole) in acetonitrile (roughly 5 mL for every gram of imidazole compound) under argon. To the mixture were added dropwise equal molar amounts of the acids (pure hydrochloric acid 37% and a *p*-toluenesulfonic acid monohydrate dispersion in a small amount of acetonitrile), the mixture was then stirred for 30 min under these conditions. Then, the mixture was heated up to 60 °C for 24 h. After that, the acetonitrile was removed by vacuum at 60 °C, all salts precipitated with the exception of [Hmim]Cl, which remained as a viscous liquid until precipitating after being washed with ethyl ether several times. All salts were washed with ethyl ether several times and then dried up by vacuum at 60 °C for several hours. The salts were stored under argon. Melting points for [NO_2Hmim]Cl and [NO_2Hmim][TsO] were 135.5-136.1 °C (decomposition occurred as well as melting) and 119.6-120.4 °C, respectively. ^{1}H and ^{13}C-NMR analyses of the compounds are shown in SI (Fig. S3-S10). FTIR spectra of [NO_2Hmim][TsO] and [NO_2Hmim]Cl are presented in Fig. S11 and S12, respectively. Most salts remained apparently unmodified after weeks of storage, with the exception of [NO_2Hmim]Cl that changed from an off-white color to slightly green.

General procedure for the acetylation of glycerol. In a Schlenk flask with a magnetic stir bar were added glycerol (0.4878 g, 5.3 mmol), catalyst and acetylating agent (2 mL, 21.2 mmol for acetic anhydride or 2.43 mL, 42.4 mmol for acetic acid). After the addition of the acetylating agent, the Schlenk flask was immediately placed in a pre-heated oil bath with magnetic stirring, covering most of the flask in oil. For entries 2, 3, 5, 6, 8, 10, 13 and 18 in Table 1, right after the end of the reaction, the whole reaction mixture was transferred to a Buchi Kugelrohr glass oven. The acetylating agent was removed under vacuum at 75 °C for 10 to 15 min. All entries then followed the same procedure; right after the end of the reaction or distillation on the glass oven, 300 mg of reaction mixture were dissolved in DMSO-d_6 to a volume of roughly 0.6 mL, placed in an NMR glass tube and then analyzed by ^{13}C-qNMR spectroscopy.

General procedure for ^{13}C-qNMR spectroscopy. Sample preparation was done as follows: a fraction of the reaction mixture with or without acetylating agent was transferred to an Eppendorf type tube, approximately 300 mg of sample was used for each analysis. This sample amount was then dissolved in DMSO-d_6 (stored on 4Å molecular sieves) to a volume of about 0.6 mL and then transferred to an appropriate NMR tube. All spectra were acquired in the same way, with a temperature of 25 °C, no spin, 240 scans, relaxation delay of 25 s, pulse angle of 90°, no NOE enhancement, spectral window from 58 to 78 ppm and 8192 data points. Auto lock and gradient shimming were used before acquiring. Mestrenova v6.0.2 – 5475 was used for data handling. All spectra were treated in the same way, zero filling to 16k, apodization was made by using the exponential function set to 1.50 Hz and the convolution difference function set to the standard values of the software. Automatic phase and baseline correction were used. To decrease the error when integrating the area of the peaks, the global spectral deconvolution (GSD) tool was used, refinement level set to 20 fitting cycles and resolution set to 0.10. Since the GSD tool generates a synthetic spectrum by deconvolution, the software can display a table with the areas of all peaks; these areas were used to calculate the relative amounts of acetins in the mixtures. The chemical shifts were corrected by setting the DMSO peak to 39.52 ppm; since the spectra were all acquired between 58 and 78 ppm, the chemical shift corrections were made by setting one full spectra by the DMSO peak and then using the acetin peaks to correct all other spectra.

Theoretical calculations. The theoretical calculations were performed for the four imidazolium salts, four ionic liquids, *p*-toluenesulfonic acid, glycerol, acetic anhydride and acetic acid optimized structures. The structures were firstly optimized using the standard settings for the classical AMBER force field as

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implemented in the GABEDIT software,[22] secondly at the Hartree-Fock/6-31+G* level of theory and, finally, at the B3LYP functional using 6-31+G* basis set with the D3BJ correction[23] in the ORCA 4.0.1.2 software.[24] IPBE were calculated using structures optimized in the TPSS-D3/6-311++G(3df,3dp) level, using structures from B3LYP-D3 as inputs. The resolution of identity approximation (Split-RI-J as implemented in ORCA) was used in the TPSS-D3 calculations in order to speed up the process. IPBE were also counterpoise corrected using a previous procedure.[25] Tight conversion settings were used in all calculations as implemented in ORCA. The initial guess of the molecular orbitals stem from the PMODEL method, as implemented in ORCA. Vibrational frequency calculations were performed in the final optimized structures to certify the minimum local state in the potential energy surface. Most of the final structures have no imaginary frequencies associated to them, with the exception of [Hmim][TsO] at the B3LYP-D3/6-31+G* level, which has a imaginary frequency at 5.89 cm^{-1}, but since this is such a small value, the structure was considered to be valid. The frontier orbital energies, CHELPG charges and bond distances for the reaction descriptors were calculated in single point runs at B3LYP-D3/6-31+G* level of theory in ORCA. Molecular electrostatic potential maps (MEPs) of total electronic densities using the partial charges were calculated at the B3LYP-D3/6-31+G* level using the Gabedit software. The isosurface value used was 0.016803 with grid values from -0.09 to 0.09. Details on the equations used to calculate the descriptors, as well as all optimized structures can be found in the supporting information.

Conflicts of interest

There are no conflicts to declare.

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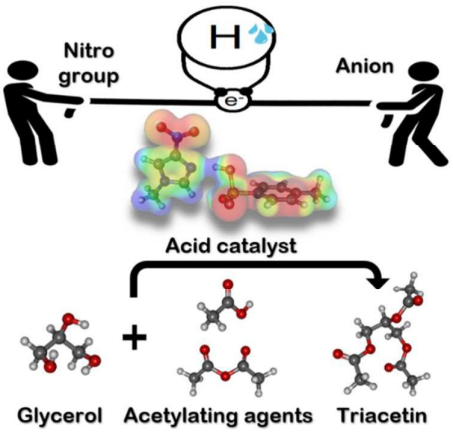

A simple and inexpensive nitration of the imidazolium cation can considerably increase its acidic activity in the acetylation of glycerol.