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Superelectrophilic activation of polyfunctional organic compounds using zeolites and other solid acids†

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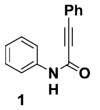
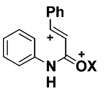
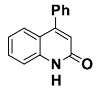
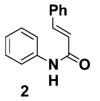
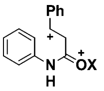
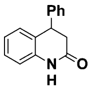
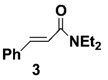
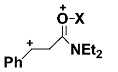
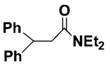
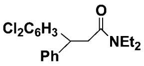
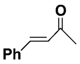
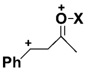
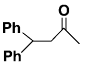
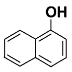
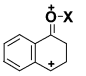
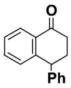
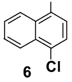
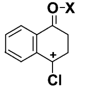
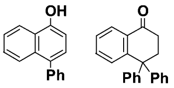
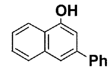
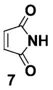
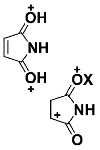
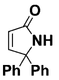
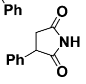
Zeolites and other available solid acids have been successfully applied to initiate reactions, which were earlier recognised to involve superelectrophilic intermediates and thus required excess of superacids to be carried out.

Superelectrophilic intermediates[1] are typically generated when a cationic electrophile is further protonated or coordinated by a Lewis acid to produce a dicationic species. Similarly, superelectrophilic solvation[2] may also involve weaker interactions without forming limiting dications resulting however in enhanced electrophilic reactivity. Recent years have seen the appearance of many useful

Table 1 Comparison of "parent" reactions with their solid acid mediated analogues

Compound treated	Superelectrophile,[a] X = H or $Al_nCl_{3n}^-$, $Al_nBr_{3n}^-$	Product	Reaction conditions, referred/**studied**	%Yield	Ref.
 1			PPA,[b] 120 °C, 0.5 h	81	9
			CF_3SO_3H, 25 °C, 100 h	97	10
			HUSY, benzene, 130 °C, 1 h[c]	95	
			Nafion SAC-13, benzene, 130 °C, 3 h[c]	70	
 2			PPA, 130 °C, 0.15 h	90	11
			CF_3SO_3H, 25 °C, 5 h	85	12
			ZrO_2/SO_4^{-2}, benzene, 120 °C, 15 h[c]	98	
			HUSY, benzene, 130 °C, 15 h[c]	90	
			HUSY, o-dichlorobenzene, 190 °C, 27 h[d]	100	
			HUSY, o-dichlorobenzene, 190 °C, 25 h[e]	20	
			HZSM-5, benzene, 120 °C, 2 h[c]	—	
			Nafion SAC-13, benzene, 130 °C, 20 h[c]	6	
 3			$AlCl_3$, benzene, 25 °C, 0.5 h	100	13
			CF_3SO_3H, benzene, 25 °C, 15 h	100	13
			HUSY, benzene, 130 °C, 70 h[c]	97	
			$AlCl_3$, o-dichlorobenzene, 25 °C, 6 h	95	13
			HUSY, o-dichlorobenzene, 190 °C, 15 h[c]	85	
 4			$AlCl_3$, benzene, 20 °C, 1 h	70	14,15
			CF_3SO_3H, benzene, 23 °C, 24 h	60	16,15
			HUSY, benzene, 130 °C, 1 h[c]	55	
 5			$AlCl_3$, benzene, 20 °C, 16 h	90	17
			$HF\text{-}SbF_5$, 0 °C, 2 h	90	17
			HUSY, benzene, 130 °C, 70 h[c]	72	
			HUSY/HCl, benzene, 130 °C, 40 h[c]	90	
 6			$HF\text{-}SbF_5$, −5 °C, 0.5 h	82[f]	17
			$AlCl_3$, benzene, 80 °C, 1 h	75	17
			HUSY, benzene, 130 °C, 3 h[c]	70	
			Nafion SAC-13, benzene, 130 °C, 15 h[c]	—	
 7			CF_3SO_3H, 20 °C, 40 h	69	18
			$AlCl_3$, benzene, 20 °C, 36 h	83	18
			$AlBr_3$, benzene, 20 °C, 4 h	95	18
			HUSY, benzene, 130 °C, 24 h[c]	95	
			Nafion SAC-13, benzene, 130 °C, 45 h[c]	—	

[a] Structures of key intermediates generally suggested for the superacid or aluminium halide mediated reactions. [b] Polyphosphoric acid. [c] The molar ratio of solid acid sites and compound treated is ~10 : 1, respectively. [d] The molar ratio of the acidic sites/compound treated is 2 : 1. [e] The molar ratio of the acidic sites/compound treated is 2 : 3. [f] The overall yield.

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† Electronic supplementary information (ESI) available: experimental details, including activation of solid acids and typical procedure. See http://www.rsc.org/suppdata/cc/b4/b404074k/

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reactions and synthetic approaches which involve superelectrophilic activation of reagents mediated by liquid superacids or by excess of aluminium halides.[1–3] Unfortunately, the procedures, often attractive for production of fine chemicals and pharmaceuticals, suffer from the significant disadvantage of using a large excess of non regenerable strong acid. Obviously, the utility of solid acids to provide these reactions is highly desirable from practical and environmental standpoints.

Recent reviews show significant progress in the application of solid acids in synthetic organic chemistry.[4] However, the scope of the reactions involves generally classical Friedel–Crafts or other acid catalysed reactions which do not require superacidity. In the present paper we report solid acid mediated reactions which occur normally only under superacidic conditions or in the presence of large excess of aluminium halide. As the acidity of solid acids such as H-zeolites, sulfated zirconias or Nafion-H is generally considered[5] to be well below that of superacids ($-12 < \mathrm{Ho} < -24$),[6] the hypothesis of identical dicationic intermediates may be easily discarded. However, the framework of a solid acid may provide close proximity of acidic sites enabling the formation of diprotonated (coordinated) species. Moreover, an effective compensation of comparatively low proton acidity of zeolites may be obtained due to nucleophilic assistance of the lattice oxygens in the transition state of a concerted mechanism resulting in an increase of the protonation rate.[5b,7] Similarly, the enzyme mediated protonation of a heterocyclic carbocation[8] provides an example showing that structural factors of acids can have a profound influence in electrophilic activation.

The reactions which we report here encompass Friedel–Crafts alkylations and cyclo-alkylations of aromatics accompanied in some cases by cationic rearrangements (Table 1). Typically, reactions were performed in high pressure tubes under stirring. Reaction mixtures, after cooling, were worked up with water and extracted with ether to isolate crude products, which were purified by silica gel chromatography or crystallisation. The solid acids were recovered and reused without loss of activity. The comparison between superacid or aluminium halide mediated reactions with those observed on solid acids shows a strong analogy. It is particularly interesting to note the reactivity of amide **3** towards *o*-dichlorobenzene, a poor nucleophile, normally inert towards monocationic C-electrophiles,[19] supporting the strong electrophilicity of key intermediates. It is also worth noting that successful results were obtained only when an effective excess of acidic sites[20] was used. Moreover, saturation of reaction mixtures with gaseous HCl appeared to be beneficial in promoting some reactions, such as reaction of 1-naphthol (**5**) with benzene. Likewise, the increased reactivity of **6** can be explained by elimination of HCl upon the reaction. These experimental data are in accord with the suggested mechanisms, involving the intermediacy of adsorbed dicationic or dicoordinated species, probably in equilibrium with their monocationic precursors. It seems reasonable, that the generation of these intermediates is a limiting step. The resulting superelectrophiles should in no way be considered as free dications but rather as intermediates stabilised by strong interaction with counterionic surface of the solid acid. The ability of HUSY and sulfated zirconias to initiate the reactions appeared to be comparable and notably higher than that of Nafion, which was successfully used only in the case of the most active compound **1**. This may be in relation with the contribution of Lewis acid sites in the activation with former acids. In agreement with this suggestion, the HUSY induced reactivity of 4-chloro-1-naphthol (**6**) is similar to its reactivity in the presence of aluminium halides, which, in contrast to Broensted superacids readily provokes the isomerization of intermediate 4-phenyl-1-naphthol into 3-phenyl-1-naphthol.[17] Analogously, the reaction of maleimide (**7**) initiated with HUSY gives the same result as obtained upon action of aluminium halides, whereas the use of exclusively protonic solid acid, Nafion does not provide any reaction.

In summary, we have shown here that solid acids instead of superacids may be successfully used to carry out some reactions proceeding only through dicharged intermediates and we suggest that similar procedures can be followed to carry out analogous reactions. Our method seems promising for practical applications because solid acids could be easily reused in contrast with superacids.

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Notes and references

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