Metal-free activation of C–C multiple bonds through halide ion pairs: Diels–Alder reactions with subsequent aromatization

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ABSTRACT

Imidazolium and ammonium halides, both in homogeneous phase or immobilized on mesoporous silica, proved able to promote the aromatization reaction of Diels–Alder adducts under ethylene and H_2 elimination. These observations point to the increased nucleophilicity of such halide ions. They also open the possibility to employ such ion pairs as nucleophilic organocatalysts, for example, as substitutes for phosphines or amines.

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Ionic liquids (ILs) have attracted much interest in recent years as they turned out to be extremely useful for a whole range of cutting edge applications.[1] Indeed, due to their very low volatility, they are presented as sustainable solvents for industrially relevant reactions,[2] allowing to isolate the products by evaporation or extraction, while possible (organo-metallic) catalysts remaining in the IL phase can be directly recycled.[3–5] Additionally, ILs can stabilize polar or charged species and reaction intermediates and are, thus, able to accelerate the rate of organic reactions through pure solvation effects.[6–8]

Nevertheless, when the products of the reaction cannot be recovered by distillation, their extraction with standard organic solvents can be difficult, which makes the sustainability of the whole process at least questionable. Therefore, many works concentrated on the development of 'heterogenised' ILs by their anchoring on high surface solids, usually silica,[9–12] or their trapping in mesoporous systems as for ionogels.[13] MCM type silica has also been made by directly using long chain imidazolium-based ILs (typically 1-hexadecyl-3-methylimidazolium chloride, C_{16}mimCl) as the templating agent.[14,15] The latter material seemed to be very convenient to test whether immobilized ILs would feature catalytic properties similar to that of the bulk equivalents. This point is not obvious, as both confinement (within mesopores)[16] and site isolation (of the catalytic species)[17,18] are known to strongly affect the catalytic activity of many systems.

Chloride and bromide are very common counter ions of cationic surfactants but in ionic liquids more complex anions are often employed (like BF_4^-, PF_6^- or bis(trifluoromethylsulfonyl)imide, NTf_2^-) to lower their melting points and/or tailor their hydrophilic/hydrophobic balance. However, since halide ions are both typical counter ions for surfactants and known to be much more nucleophilic (and were thus shown to alter the observed reactivities in halogenated ILs[19]), we preferred to choose halides as counter ions for this study. We therefore evaluated the capacity of C_{16}mimCl immobilized in MCM-48 (prepared as previously described[14,15]) type silica (C_{16}mimCl@MCM-48, Fig. 1) to promote Diels–Alder[20–22] type [4 + 2] cyclo additions, as they were already shown to be strongly accelerated by ILs.[8] Other reports, however, state that chloride containing ionic liquids lower the yield and selectivity of Diels–Alder reactions due to their ability to act as strong hydrogen bond acceptor.[23]
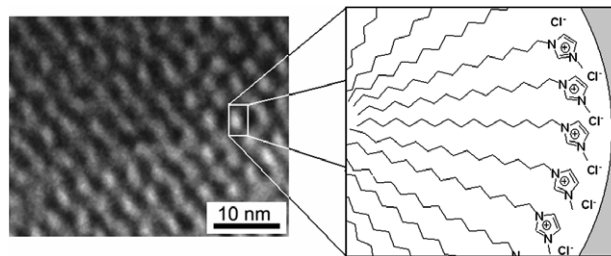

Figure 1. Transmission electron micrograph and schematic representation of C_{16}mimCl@MCM-48, one of the catalysts we employed.

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We tested a variety of possible dienes and dienophiles. In most cases, our solid had no influence on the outcome of the reaction. Moreover, under the chosen moderate conditions mostly no reaction was observed at all. However, our interest was attracted by the reaction of naphthoquinone and benzoquinone with 1,3-cyclohexadiene (Scheme 1).

In the first case, a 100% conversion of the reactants was observed. However, instead of the expected cyclo addition product (1,2,3,4,4a,9a-hexahydro-1,4-etheno-anthraquinone, **1**, which is the only product obtained when no salt is added under the same reaction conditions), anthraquinone was observed as the major product. The formation of anthraquinone is also observed with benzoquinone (in even higher yields). The diaddition product is not detected in the non catalyzed reaction, and no elimination of the 1,4-etheno-bridge was observed.

Obviously, a formal elimination of ethene and hydrogen takes place under our reaction conditions. In the case of benzoquinone, the second addition presumably takes place after the first aromatization step toward naphthoquinone. Indeed no double aliphatic addition product (i.e., no compound with two bicyclic groups) is detected. Moreover, reference tests with non-immobilized C_{16}mimCl also showed the occurrence of dealkylation, while only the immobilization within SiO_2 enabled diaddition.

In order to test the versatility of this reaction, various combinations of dienes and dienophiles (all featuring carbonyl functions as they seem essential to observe the aromatisation product) have
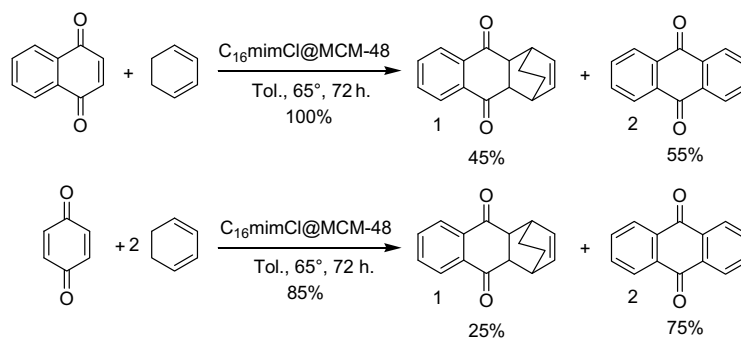
Scheme 1. Diels–Alder cyclo addition of naphthoquinone on cyclohexadiene catalyzed by C_{16}mimCl@MCM-48.

Table 1
Other Diels–Alder type reactions in presence of C_{16}mimCl@MCM-48[a]

Entry	Dienophile	Diene	Extend of conversion[b] (%)	Product distribution[b] (%)
1			66	100%
2			100	100%
3			100	92% 8%
4			100	100%
5			40	91% 9%

[a] Reaction conditions: 2 mmol of substrate, 0.1 g of C_{16}mimCl@MCM-48 (0.15 mmmol C_{16}mimCl), in toluene (2 ml) at 65 °C for 72 h.
[b] Conversion rates and product distribution were determined by ^{1}H NMR.

been tested under similar conditions. The obtained results are summarized in Table 1. As can be seen, it turned out that a couple of Diels–Alder addition products were able to undergo either dehydrogenation (when butadiene or dimethylbutadiene is used) or a dealkylation to yield aromatic species even if some yields remained low.

The reaction was analyzed in more details to shed some light on the actual mechanism. In order to decouple the various factors impacting the observed reactions, we presynthesized the Diels–Alder product **1** and submitted it to various possible catalysts or catalyst components (such as C_{16}mimCl@MCM-48, calcinated mesoporous silica without IL, and non-immobilized ILs with different counterions, etc.) in toluene at 65 °C for 72 h. Under the term catalyst, we mean here a compound which can promote the aromatisation reaction, being understood, that our salts have only a minor effect on the first Diels–Alder step. Since certain ILs are not soluble in toluene, reactions were also carried out in acetonitrile as the solvent. Table 2 summarizes the obtained results. Immobilized ions pairs all proved able to yield the aromatization product in moderate yields. The obtained conversions were relatively modest as compared to those reported in Scheme 1. This can, on the one hand, be explained by diffusion limitations. Indeed, access to the active pores of C_{16}mimCl@MCM-48 is more difficult for the relatively bulky compound **1** than for naphthoquinone or cyclohexadiene. But, on the other hand, the fact that non supported ion pairs proved even less active than immobilized ones also points out the synergetic role of silica (e.g., supported CTAC (Table 2, entry 27) yielded 27% of anthraquinone in acetonitrile while the same salt without silica only yielded 9% of product under otherwise similar reaction conditions). The origin of this effect of silica still has to be studied in detail, which would add a stone to the current work on the often observed confinement effects in porous catalysts.[16] Silica alone (without ion pairs) (Table 2, entry 6), however, was not able to promote the expected reaction. In the case in which the washed C_{16}mimCl@MCM-48 (obtained by a 12 h Soxhlet extraction with acetone as a solvent) was used (Table 2, entry 7), a thermogravimetric analysis of the resulting powder showed that only about 50% of the salt had been removed. This possibly facilitated the diffusion of the reactants through the solid, accounting
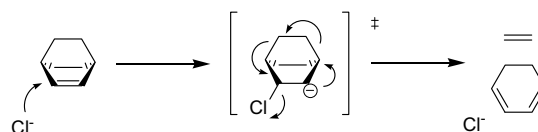
for the enhanced activity of this solid. In some tests with supported ion pairs, minor leaching could be detected (either in the GC–MS chromatograms or in the NMR spectra, see supporting information), but evaluating the actual impact of this leaching was difficult and would require more detailed investigations.

As can be seen, in the case of non-immobilized ILs, a reasonable amount of dealkylation compound was observed as soon as the IL is miscible with the solvent and its anion is a halide. For example, C_4mimCl yielded 10% of anthraquinone in acetonitrile while C_4mimBF$_4$ (also soluble in acetonitrile) failed to provide any detectable reaction. This suggests that, solubility provided (NaCl, for example was not soluble in either solvent and only yields traces of dealkylation product (Table 2, entry 12)), dealkylation is primarily driven by the halide counter ion, while the nature of the cationic amine (either an imidazolium (Table 2, entries 8, 10, and 11) or an ammonium (Table 2, entry 9)) only plays a secondary role. Interestingly, when the dealkylation reaction of **1** was run in pure C_4mimCl as both the solvent and the catalyst under otherwise identical reaction conditions only 1% of dealkylated product could be extracted.

The physical properties of ILs with halide ions as counterions already give first indications to understand their special role in this reaction. Indeed, Armstrong et al. analyzed the solvatation properties of various ILs using a multiple parameter approach and found imidazolium halide based ILs to be among the most polar and hydrogen-bond basic ILs.[19] This is in agreement with the increased nucleophilicity of halide ion containing ILs, as also stated by Aggarwal et al.[23] While the strong nucleophilicity of ILs can lower their catalytic activity due to a strong interaction with the cation of the IL, it is known that strong nucleophiles can add to activated C–C multiple bonds to form anionic or zwitterionic species. Dimethyl acetylene dicarboxylate (DMAD) has, for example, been reported to undergo attacks from DABCO or even pyridine.[24,25]

A possible mechanism for the dealkylation of [2,2,2] bicyclooctene derivatives could thus involve the attack of the chloride on the C=C double bond, followed by a pericyclic shift of C–C bonds, resulting in a formal retro-Diels–Alder reaction (See Scheme 2).

The possibility for a bicyclic molecule to undergo such an aromatization would then directly depend on the ease with which the chloride anion can attack its double bond, that is on the polarizability thereof. And actually, the polarizability of such C=C

Table 2
Conversion of **1** into anthraquinone by various salts[a]

Entry	Salt	Amount of anthraquinone in toluene[b] (%)	Amount of anthraquinone in acetonitrile[b] (%)
1	–	0	0
2	C_{16}mimCl@MCM-48	13.5	20
3	C_{16}mimBr@MCM-48	31	33
4	CTAC@MCM-48	25	27
5	CTAB@MCM-48	21	19
6	SBA-15 type, calcined	0	0
7	Washed C_{16}mimCl@MCM-48	33	40
8	C_{16}mimCl	2	19
9	CTAC	4	9
10	C_4mimCl	1	10
11	C_4mimBr	0	3
12	NaCl	Traces	Traces
13	C_4mimBF$_4$	0	0
14	C_4mimPF$_6$	0	1

[a] Reaction conditions: 0.2 mmol of **1**, 0.05 g of possible catalyst, in 2 ml solvent, at 65 °C for 72 h.
[b] The amount of formed anthraquinone was determined by ^{1}H NMR. (See supplementary information.)

Scheme 2. Putative mechanism for the chloride catalysed dealkylation of a formal [2,2,2,] bicyclooctene.
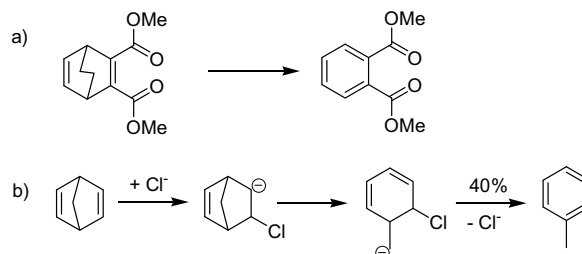
Scheme 3. Other C_{16}mimCl catalyzed bicycle openings.

double bonds can be affected by various factors such as the presence of carbonyl groups, but also the presence of other C=C double bonds in a close neighborhood or the tension within the cycle. This is in good agreement with the results reported in Table 1 as well as with the following observations: dimethyl-[2,2,2]-bicyclooctadiene dicarboxylate could be quantitatively converted into dimethylphthalate when treated with C_{16}mimCl in methanol for 24 h (Scheme 3a) and norbornadiene ([2,2,1]-bicycloheptadiene) was converted into toluene when submitted to a similar reaction environment (Scheme 3b). In the latter case, no carbonyl group seems to be required to observe a transformation. However, the compound is already a diene and the methylene bridge imposes a strong constrain on the cycle, which is eased by the isomerisation. Furthermore, an isomerisation was observed in state of a dealkylation because the release of a formal methylene group would be very unfavorable. It is worth being noticed here that for commodity reasons these additional tests were run without the silica support. Indeed, the use of MCM-48 strongly increases the complexity of the system, adding considerations of diffusion limitations, confinement, etc. As this report focuses on the first observations of such an aromatization process, simplicity was required. We thus focused on solubilized ions pairs. All these observations, however, are in good agreement with our proposed bond attack of the chloride. Nevertheless, further theoretical investigations are required to assess a more detailed reaction mechanism and additional experiments would be required to address the actual role of porous silica.

This vision of an anion induced retro-Diels–Alder reaction adds to a longer discussion on the usually admitted concerted orbital control of this type of reactivity. The classical mechanistic view on Diels–Alder reactions was nicely reviewed by Sauer and Sustmann.[26] Schleyer et al., however, pointed out that for polarisable starting products a two-step pathway essentially involving a zwitterionic intermediate was energetically more favourable than the Woodward-Hoffmann route.[27] In 1993, Reetz and Gansauer found that a heterogenous dispersion on Lithium perchlorate was able to catalyse Diels–Alder reactions and regioselective 1,3-Claisen rearrangements,[28] a system which was already quite closely related to the present observations. Meanwhile, there is collected theoretical and experimental evidence that at least Diels–Alder reactions with more polarizable reactants progress along a two-step mechanism involving a charged or zwitterionic intermediate (e.g., see Refs. [29–32]). On the other hand, as only a limited number of systems seem to undergo zwitterionic activation, it appears that this mechanism is more an additional reaction channel, i.e., an alternative to the usual case of concerted orbital controlled cyclo addition. Nevertheless, these observations open some promising opportunities for the metal-free functionalization of C=C double bonds, as the anionic intermediate could react for instance in a Knoevenagel-like fashion (in which it would deprotonate the nucleophile and then act as an electrophile) or in Morita-Baylis-Hillman reactions.

Acknowledgement

Supplementary data

Detailed catalytic procedures as well as a typical example of ^{1}H NMR spectrum are presented. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.05.027.

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