Friedel–Crafts reactions in room temperature ionic liquids

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Friedel–Crafts reactions in the ionic liquid system 1-methyl-3-ethylimidazolium chloride–aluminium(III) chloride can be performed with excellent yields and selectivities, and in the case of anthracene, have been found to be reversible.

The possibility of carrying out chemical transformations in low temperature ionic liquids has, to date, received little attention.[1] Ionic liquids such as the [emim]Cl–AlCl$_3$ ([emim]$^+$ = 1-methyl-3-ethylimidazolium cation) system have been shown to demonstrate catalytic activity in reactions such as Friedel–Crafts acylations,[2,3] alkylation reactions,[4] isomerisation of alkanes,[5] and the alkylation of isobutane with butene.[6] Here, we present a series of reactions of AcCl with carbocyclic aromatic compounds in acidic compositions (X = 0.67)‡ of [emim]Cl–AlCl$_3$ (Fig. 1) and compare their performance with similar reactions in 'conventional' molecular solvents.

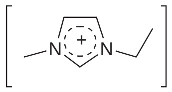


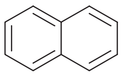
Fig. 1 The structure of the [emim]$^+$ cation

To date, there have been very few publications detailing reactive chemistry in ionic liquids.[1] With the development of ambient temperature ionic liquids, the possibility of investigating chemical processes in these new solvents provides an interesting challenge. One of the most studied ionic liquids is the [emim]Cl–AlCl$_3$ system.[7,8] An investigation of the Friedel–Crafts reactions of simple benzene derivatives in this medium has been performed by Wilkes.[3] With a view towards developing reactions for clean synthesis in ionic liquids, a number of Friedel–Crafts acetylation reactions have now been performed. The Friedel–Crafts reactions of five simple aromatic compounds has been investigated and are shown in Table 1.

The reactions work efficiently, giving the stereoelectronically-favoured product. In the acetylation reaction of naphthalene **1**, the major product was the thermodynamically unfavoured 1-isomer, with a 2% yield of the 2-isomer. This is in accordance with best literature yield and selectivity.[9,10] It has been suggested that the position of attack on naphthalene is determined to a large extent by steric factors.[11] For example, if the reaction is carried out in nitrobenzene or nitromethane,[11] the 2-isomer is the major product and the acylating agent is thought to be an AcCl–AlCl$_3$–nitrobenzene complex. In the ionic liquid, the acylation agent is thought to be the free acylium ion.[3,12,13] Since the acylium ion is much smaller than the adduct, attack at sterically more hindered positions can occur.[3,13] In the ionic liquid, subsequent rearrangement of 1- or 2-acetylnaphthalene was not observed to occur. This was confirmed when the products were heated to 100 °C and in the presence of added hydrogen chloride,[14] and no further reaction was observed. In the acetylations of toluene **2**, chlorobenzene **3** and anisole **4**, all the major products were the 4-isomers. In these cases, the 2-isomers were present, but at levels less than 2%. These yields and selectivities were as good as the best published results.[15–17] With the reaction of 1,1,2,6-tetramethyl-3-isopropylindane **5**, the fragrance traseolide (5-acetyl-1,1,2,6-tetramethyl-3-isopropylindane) was obtained in 99% yield as a single isomer. The stereochemical arrangement of the indane ring was unaffected by the reaction.

Table 1 Friedel–Crafts acylation of aromatic compounds **1–5** with AcCl in [emim]Cl–AlCl$_3$ (X = 0.67)

Aromatic compound	T/°C	t/h	Products (% yield)
1	0	1	1-AcAr (89), 2-AcAr (2)
2	20	1	4-AcAr (98), 2-AcAr (1)
3	20	24	4-AcAr (97), 2-AcAr (2)
4	−10	0.25	4-AcAr (99)
5	0	1	5-AcAr (99)



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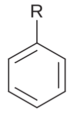
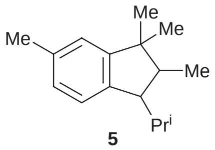


2 R = Me
3 R = Cl
4 R = OMe



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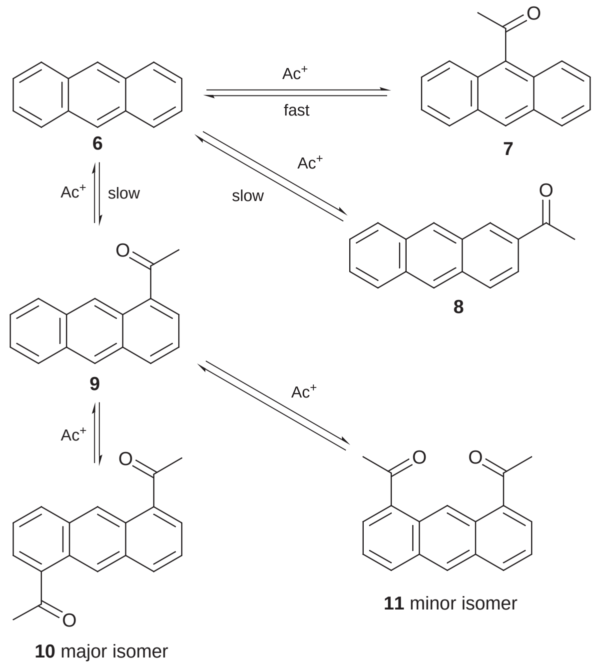
The acetylation reactions of anthracene were found to behave in a different manner to those of simpler aromatic compounds. Anthracene is generally considered to undergo acetylation reactions primarily at the 9-position.[18] Furthermore, the possibility of diacetylation exists, and deacetylation reactions complicate the chemistry, leading to a complex mixture of products. Owing to the complexity of the reaction, it was decided to monitor the variation of composition of the reaction mixture with time by gas chromatographic analysis.

It can be seen from Table 2 that 9-acetylanthracene **7** is the initial product in the reaction, formed rapidly in under 5 min, but this subsequently undergoes a slow disproportionation to anthracene and the two isomers of diacetylanthracene, **10** and **11**. Also, small amounts of 1- and 2-acetylanthracene are formed transiently. This implies that the monoacetylation of anthracene is reversible. Since the 1,5- and 1,8-diacetylanthracenes are the only isomers found in the final products, only the 1-acetylacthracene intermediate can undergo diacetylation. A plausible mechanistic scheme for this reaction is given in Scheme 1.

Table 2 The acetylation of anthracene **6** in [emim]Cl–AlCl$_3$ (X = 0.67) at 0 °C

		Composition (%)			
Reaction time	AcCl/equiv.	**6**	**7**	**10**	**11**
5 min	1.1	23	69	0	0
24 h	1.1	34	0	32	24
5 min	1.5	15	73	3	1
24 h	1.5	25	0	42	33
5 min	2.1	13	69	5	3
24 h	2.1	1	1	57	42

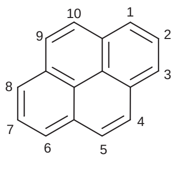


Scheme 1

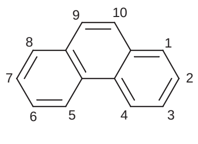
It was decided to investigate the behaviour of 9-acetylanthracene in the ionic liquid. 9-Acetylanthracene dissolves in the [emim]Cl–$AlCl_3$ ($X = 0.67$) ionic liquid at 0 °C, and undergoes a slow conversion to anthracene (33%), **8** (12%), **10** (31%) and **11** (22%) (Scheme 1). Initially, a very slow reaction was observed. When a proton source (water) was introduced to the reaction vessel, a more rapid reaction occurred suggesting a proton-catalysed mechanism. The addition of small quantities of water to the reaction vessel leads to the formation of hydrogen chloride, which in chloroaluminate ionic liquids behaves in a superacidic manner.[14]

From these observations, it is possible to propose a plausible mechanism for the behaviour of 9-acetylanthracene in [emim]Cl–$AlCl_3$ ($X = 0.67$). It behaves in a manner that is very similar to that shown in Scheme 1. The key initial step must involve the protonation of **7** followed by loss of the acylium ion.

The acetylation reactions of pyrene and phenanthrene were also investigated (Table 3). The reaction of pyrene with AcCl in the ionic liquid appeared to behave in a similar manner to that of anthracene. The major products were the 1,6- and 1,8-isomers of diacetylpyrene, **12** and **13**, and the minor product was identified as 1-acetylpyrene **14**. This behaviour has not been reported in previous acetylation studies.[19] In the acetylation of phenanthrene, the mono-acetyl derivatives are the major products, with very little of the diacetyl products formed. As expected, 9-acetylphenanthrene **15** is the major product, and the minor products are the 1- and 2-isomers, **16** and **17**. This is very similar to conventional $AlCl_3$ catalysed reactions of AcCl with phenanthrene.[20]



12 1,6-Ac_2
13 1,8-Ac_2
14 1-Ac



15 9-Ac
16 1-Ac
17 2-Ac

Based on these initial results, ionic liquids appear to provide an excellent medium for performing Friedel–Crafts reactions. Simple aromatic compounds, such as toluene, anisole or chlorobenzene are easily acetylated in yields that are equal to the best literature yields.[9–14] In addition, the regiochemical control of these reactions is excellent. In the acetylation of electron-rich polyaromatics, there is evidence that the reaction is reversible and that deacetylation reactions are proton catalysed. As for the mechanism of these reactions, the reaction of naphthalene appears to show that the acetylating agent is sterically small, and is probably the free acylium ion. It should also be noted that carbocyclic aromatics, such as naphthalene, phenanthrene and pyrene, form highly coloured compounds in acidic [emim]Cl–$AlCl_3$, probably π-complexes as they are paramagnetic.[21,22] The fact that paramagnetic species are present, and that protons play a significant part in these reactions, suggests that the classical mechanisms proposed for the Friedel–Crafts reaction may need modification.

Table 3 The acetylation of pyrene and phenanthrene in [emim]Cl–$AlCl_3$

Aromatic compound	T/°C	Time	AcCl/ equiv.	Starting material	Composition (%)
					Products
Pyrene	20	2 h	1.2	32	13 (**14**), 55 (**12** + **13**)
Phenanthrene	−10	5 min	1.5	0	55 (**15**), < 5 (**17**), 30 (**16**)

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Notes and References

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‡ The composition of a tetrachloroaluminate(III) ionic liquid is best described by the apparent mole fraction of $AlCl_3$ [$X(AlCl_3)$] present. Ionic liquids with $X(AlCl_3) < 0.5$ contain an excess of Cl^- ions over $[Al_2Cl_7]^-$ ions, and are called 'basic'; those with $X(AlCl_3) > 0.5$ contain an excess of $[Al_2Cl_7]^-$ ions over Cl^-, and are called 'acidic'; melts with $X(AlCl_3) = 0.5$ are called 'neutral'.

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