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FRIEDEL-CRAFTS REACTION OF α-CHLOROALDIMINES : POSSIBLE INTERMEDIACY OF α-IMIDOYLCARBENIUM IONS

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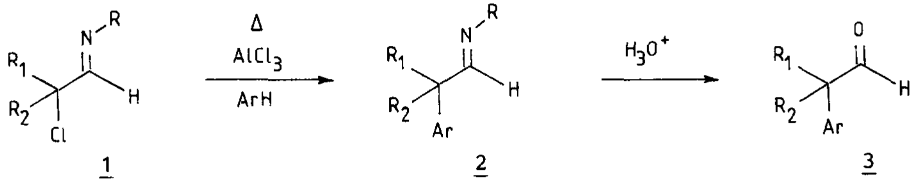
Abstract : α-Chloroaldimines are arylated at the α-position under Friedel-Crafts conditions via intermediacy of α-imidoylcarbenium ions.

α-Arylation of carbonyl compounds is an interesting synthetic process and has found widespread application, because α-arylated carbonyl compounds are useful substrates for a variety of synthetic goals, including drugs[1] and natural products.[2]

We have found that α-chloroaldimines 1,[3,4] readily available from aldehydes, in a Friedel-Crafts reaction with arenes (benzene, toluene, p-xylene) in the presence of aluminium trichloride are converted into α-arylated aldimines 2, precursors of α-arylated aldehydes 3 (Table). N-Isopropyl-α-chloro-α-phenylaldimine 1 (R_1=Me; R_2=Ph) was cleanly converted (80-82%) into α-arylated aldimines 2a,b by reaction with benzene or toluene in the presence of 2 molar equiv. of aluminium trichloride (RT 3-5 h). Aliphatic aldimines 1 (R_1, R_2, R= alkyl) are less reactive as arylation occurs only at higher temperature at a reasonable rate, but dehydrohalogenation to afford α,β-unsaturated aldimines 7 becomes a competitive reaction (10-15%; except for entry g). However, higher homologues, e.g. 1 (R_1=R_2=Et; R=i-Pr), gave elimination of hydrogen chloride exclusively. If α-arylated aldehydes 3 are the objective, it is not necessary



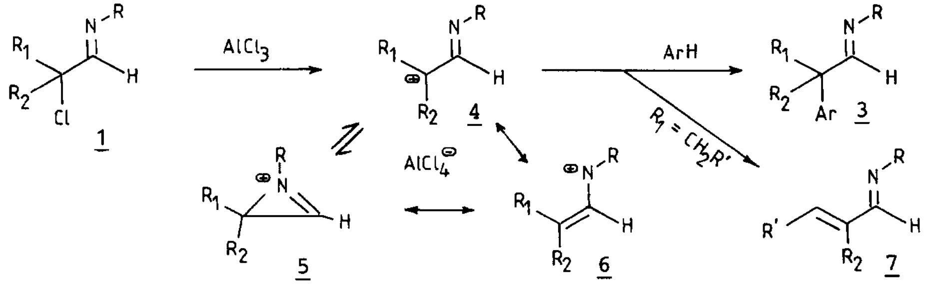
to isolate α-arylaldimines 2 as hydrolysis of the latter crude material with aqueous hydrogen chloride affords α-arylaldehydes 3 (26-40% overall yield).

Table : Friedel-Crafts Reaction of α-Chloroaldimines[13]

	R_1	R_2	R	Ar	Reaction[a] Conditions	Yield	bp °C/mmHg
a	Me	Ph	i-Pr	Ph	2 equiv. $AlCl_3$/RT 5h	80%	-[b]
b	Me	Ph	i-Pr	p-tolyl	2 equiv. $AlCl_3$/RT 3h	82%	-[b]
c	Me	Me	i-Pr	Ph	1.1 equiv. $AlCl_3$/Δ reflux 1h	32%	45- 50/0.05
c	Me	Me	i-Pr	Ph	1.1 equiv. $AlCl_3$/50°C/24h	35%	-[c]
d	Me	Me	i-Pr	2,5-$Me_2C_6H_3$	1.1 equiv. $AlCl_3$/Δ reflux 1h	29%	75- 85/0.08
e	Me	Me	i-Pr	p-tolyl	1.1 equiv. $AlCl_3$/Δ reflux 2h	26%[d]	112-115/15[d]
f	Et	Me	i-Pr	Ph	1.1 equiv. $AlCl_3$/Δ reflux 1h	40%[d]	111-114/15[d]
g	Et	Et	i-Pr	Ph	1.1 equiv. $AlCl_3$/Δ reflux 1.5h	-[e]	-[e]

[a] The arene was used as solvent; [b] Purified by column chromatography (Neutral aluminium oxide, ether:pentane 1:1); [c] α-Phenylaldimine 2c was accompanied by 1-isopropyl-3,3-dimethylindoline (12%; bp 69-74°C/0.06 mmHg); [d] Yield and bp of the corresponding aldehyde, obtained after hydrolysis with 6N HCl; [e] Dehydrochlorination exclusively to afford 60% isolated yield of N-(2-ethyl-2-buten-1-ylidene)isopropylamine 7 (R'=Me; R_2=Et; R=i-Pr; bp 53-55°C/15 mmHg).

The arylation of α-chloroaldimines 1 is most reasonably explained in terms of the intermediacy of an α-imidoylcarbenium ion 4, which is intercepted by the arene to yield 3 or is stabilized by expelling a proton to afford α,β-unsaturated aldimines 7. The corresponding oxygen analogues, i.e. α-acylcarbenium ions,[5,6] have long been ignored as possible structural entities because of the repulsive electrostatic effects of the carbenium center and the adjacent



carbonyl group. Recently, considerable interest arose for these reactive intermediates as they seem to play an important role in several reactions.[5,6]

Similar considerations concerning stability are valid for α-imidoylcarbenium ions. According to ab initio calculations,[7] bridged species 5 are more stable than the planar structures. At present, no conclusions can be drawn about the definite structure of α-imidoylcarbenium ions

The reactions described in this report are a simple entry into the chemistry of α-imidoylcarbenium ions. Further experiments are in progress to substantiate the occurrence of the latter species in reactions of a variety of α-halogenated imino compounds.

The results presented here are the first examples of a Friedel-Crafts reaction at the halogenated α-position of masked aldehydes. α-Halogenated aldehydes itself do not afford α-arylation but are known to give condensations with arenes at their carbonyl site, the most widespread reactions being the syntheses of DDT, DDD and analogues.[8] Little is known about Friedel-Crafts reactions with α-halogenated carbonyl compounds except for α-arylations of some activated (mostly phenyl substituted) α-haloketones.[5,9]
α-Arylation of imines via α-halogenated imino compounds[10] has not been reported hitherto except for α-chloro nitrones[11] and α-bromo hydrazones[12 a-d], which react in specific ways (e.g. via azoalkenes)[12e] to α-arylated derivatives.

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13. All compounds have been fully characterized by spectrometric methods (NMR, IR, MS) or by comparison with known compounds.

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