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ORGANIC FUNCTIONAL GROUP EXCHANGE CATALYSED BY INORGANIC SALTS

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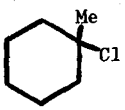
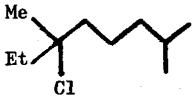
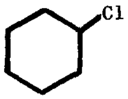
Because of steric factors the exchange of a functional group at tertiary saturated carbon is a difficult synthetic operation, often requiring forcing conditions, which encourage side-reactions such as β-elimination. We have discovered that inorganic salt catalysis offers a potentially general solution to this problem and in this paper illustrate our results by describing conditions in which the chlorine of tertiary organic chlorides can be exchanged by iodide ion.

Our route is based on the well established (Finkelstein) exchange reaction of organic chlorides with iodide ion, using sodium iodide in acetone[1]. Unfortunately, this exchange fails[1] for tertiary chlorides, but the directness and convenience of the procedure made it seem worthwhile adapting it so that steric hindrance at the functionalised carbon would not inhibit the exchange. Initially we have investigated the effect of potential Lewis acid catalysts upon the exchange. Thus, when t-butyl chloride is stirred in a non-polar solvent at room temperature with an excess of sodium iodide and a trace of ferric chloride, it is converted quantitatively into t-butyl iodide. Subsequent studies with other halides have revealed that this exchange procedure is quite general for hindered chlorides, although it can take several hours to proceed to completion. Simple primary and secondary alkyl chlorides, however, do not react. Our results are summarised in the Table, from which it will be clear that the starting chloride must either be tertiary, or benzylic in order to be exchanged. The present work therefore forms a convenient complement to the sodium iodide in acetone exchange procedure.

At first sight, catalysis of the exchange by ferric chloride seemed likely to be due to its function as a Lewis acid. However, failure of reactions in which either aluminium chloride replaced ferric chloride or sodium cyanide replaced sodium iodide, indicated that this might not be the case. Since iodide ion and ferric chloride undergo a redox reaction (albeit not to completion within the reaction times described in the Table) in these systems, an attractive alternative seemed to be the involvement of organic radical intermediates. However, radical coupling or disproportionation products are not formed in the reaction, and moreover extensive efforts to detect radicals such as the t-butyl radical were fruitless.

TABLE: Alkyl Iodides[a] from Iodide Ion (2 moles) in the Presence of Inorganic Catalysts (0.02 moles) at 20°C.

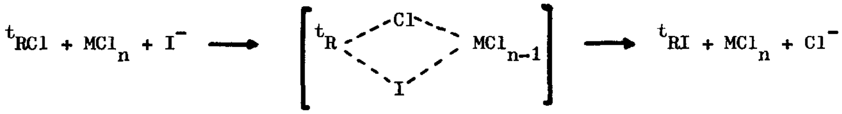
Organic Chloride	Iodide % Yield[b]	Catalyst	Reaction Time (h)
	100	$FeCl_3$	22
	98	"	72
$PhCH_2Cl$	95	"	10
$PhCHCl_2$	100	"	28
$PhCMe_2Cl$	100[c]	"	2
^tBuCl	99	"	2
^tBuCl	98	$HgCl_2$	120
	zero	$FeCl_3$	120
$ClCH_2CH_2Cl$	zero	$FeCl_3$	120

[a] isolated by standard methods and characterised fully by analysis and/or by spectroscopy.

[b] estimated by n.m.r.

[c] product not stable to reaction conditions

Further studies of these exchanges have shown that when t-butyl chloride is treated with sodium iodide and ferric chloride in benzene, the major product is t-butyl iodide (93-98%). In the absence of iodide ion, t-butylated benzenes are formed rapidly and quantitatively, as one would expect from the literature[2]. Furthermore, it has subsequently been demonstrated that ferric chloride can be replaced by mercuric chloride, and the procedure still result in efficient formation of t-butyl iodide, although no redox reaction appears to be occurring in the mercuric chloride reaction. Moreover, these iodide exchanges fail completely when sodium iodide is replaced by a soluble iodide, such as tetrabutylammonium iodide. Thus it appears that these exchanges involve not an electron transfer process, but a very intimate form of Lewis-acid catalysis, in which the ionisation of the tertiary chloride and the transfer of the iodide ion occur in a closely held complex or ion-pair, such as that represented below.



$$^{t}RCl + MCl_n + I^- \longrightarrow \left[{}^{t}R \overset{Cl}{\underset{I}{\diamond}} MCl_{n-1} \right] \longrightarrow {}^{t}RI + MCl_n + Cl^-$$

Exchange of tertiary alkyl chlorides with iodide ion (M = metal)

Such a situation is not without precedent, and has been discussed in connection with the alkylation of t-butyl chloride by metal alkyls. For example, the methylation of t-butyl chloride by trimethylalluminium has been suggested[3] to involve either an intimate ion pair, or a transition state such as that shown above. Indeed, recent reviews[4] of transition-metal catalysis of oganic reactions have underlined the possible generality of ligand transfers of the type discussed here and elsewhere[3]. The preliminary results reported here emphasise the potential value of this type of inorganic catalysis to synthetic organic chemists, and examples of other useful exchange systems will be published shortly. The mechanistic aspects of this work also appear to be of fundamental interest, and are the subject of further study.

References

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2. A good source of general information in this area is "Friedel Crafts and Related Reactions" ed. G.A. Olah, Interscience, New York, 1963. Of particular relevance are Vol. 1, Chapter IV, p279 (G.A. Olah), and Vol. II, Chapter XVII, p417 (F. Drahowzal).
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4. D.G.H. Ballard, Chem. Brit., 1974, 20; P.S. Braterman and R.J. Cross, Chem. Soc. Rev., 1973. 271