AROMATIC CHLORINATION REACTIONS WITH TITANIUM TETRACHLORIDE IN THE PRESENCE OF PEROXY ACIDS

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The chlorination of aromatic compounds by means of transition metal chlorides such as SbCl₅, MoCl₅, VCl₅ and FeCl₃ is well documented.^{1,2} The use of TiCl₄ as a chlorinating agent itself has not been reported, although it has been used as a catalyst and solvent in chlorination reactions of aromatic rings by other transition metal chlorides.³ We now report that TiCl₄ is an efficient chlorinating agent in the presence of either trifluoroperacetic acid or <u>m</u>-chloroperbenzoic acid.

Treatment of a 3-mM solution of benzene and TiCl_4 in dry dichloromethane with an equimolar amount of anhydrous trifluoroperacetic acid⁴ (0^o for 4 hours) gave, after aqueous work-up, a 60% yield of chlorobenzene, as determined by GLPC. The residue contained unreacted benzene, with no detectable dichlorobenzene. The table contains details of the major products from various acetanilides, under the above reaction conditions.

REACTANT	PRODUCTS	YIELD*	COMMENTS
Acetanilide	4-Chloroacetanilide 2,4-Dichloroacetanilide	48% 29%	
Acetanilide	4-Chloroacetanilide 2,4-Dichloroacetanilide	32% 51%	With anhydrous sodium acetate
Acetanilide	2,4-Dichloroacetanilide	97%	With EtuNCl, 5 10-fold excess
N-Methylacetanilide	4-Chloro-N-Methylacetanilide	80%	
<u>p</u> -Acetotoluidide	2-Chloro-4-Methylacetanilide	62%	

*Yields are based on starting aromatic substrate, and are determined by isolation of the products, using preparative TLC. In some cases the reaction also produced a minor product that is not a chlorinated acetanilide. Work on the structures of this product is in progress.

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The product distribution of the reaction with acetanilide was reversed on addition of sodium acetate buffer. The addition of Et_{4} NCl as a soluble source of chloride anions produced an essentially quantitative yield of 2,4-dichloroacetanilide. Replacement of the trifluoroperacetic acid with <u>m</u>-chloroperbenzoic acid gave 4-chloroacetanilide (72%) and 2,4-dichloroacetanilide (10%). A 95% recovery (based on peracid used) of <u>m</u>-chlorobenzoic acid was made. It thus appears that the chlorination reaction is readily subject to experimental control, and could be of synthetic use because of the mild conditions used.

At this stage little can be said about the mechanism of the chlorination reaction. It is known that acetanilide and TiCl_4 form a complex.⁶ We believe that the reaction is an electrophilic substitution process, involving a positive chlorine species which can be liberated from the Lewis acid by the peroxy acid. As it appears likely that more than one mole of "Cl⁺" can be liberated, this must come about by reduction of the titanium. It should be noted that the predominance of disubstitution and apparent complete lack of any <u>ortho</u>-substituted products contrasts with other chlorination reactions.^{7,8} Further work on the scope and utility of the reaction is in progress.

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