

# DEQUATERNIZATION OF AMMONIUM SALTS BY NUCLEOPHILES

Tse-Lok Ho

Department of Chemistry, University of Manitoba  
Winnipeg, Manitoba, Canada

Recently we have demonstrated the dealkylation of quaternary ammonium compounds by 1,4-diazabicyclo[2,2,2]octane.<sup>1</sup> It is believed that an alkyl exchange is involved in this reaction. With the objective of further developing new dequaternization methods, a number of nucleophiles has since been examined for their effectiveness. This communication discloses our results of this investigation.

In order to obtain a uniform picture concerning the effectiveness of various reagents, phenyltrimethylammonium iodide has been chosen as the common substrate. We have now found that demethylation occurs readily in refluxing dioxane or N,N-dimethylformamide, in the presence of a diverse array of nucleophilic agents such as triphenylphosphine, thiourea, sodium thiosulfate and sodium azide. Yields of N,N-dimethylaniline are generally better in the DMF runs, and there is no reaction in boiling ethanol.

All the above-mentioned compounds are well-known nucleophiles which react smoothly with alkyl halides, however, their potential usefulness in dealkylation of ammonium salts has not been explored. Our present survey indicates that dequaternization may be accomplished by most of

HO

the common nucleophiles at moderate temperatures, although tertiary amines are poorer leaving groups compared with halide ions in the  $S_N2$  reactions.

The general procedure for demethylation involves boiling the ammonium salt (1 mmol) with the reagent (1 mmol) in DMF or dioxane (2 ml) for 2 to 3 hours. The cooled mixture was poured into water (10 ml) and extracted with benzene (30 ml). After two aqueous washings, the benzene solution was dried ( $MgSO_4$ ) and evaporated to give the tertiary amine which was identified by comparison with an authentic sample. Tlc and spectrally pure material has been obtained routinely, except when triphenylphosphine was used. In that case simple aqueous acid extraction of the benzene solution permitted the isolation of pure product.

Table. Demethylation of Phenyltrimethylammonium iodide

Reagent	% Yield, N,N-Dimethylaniline	
	A <sup>i</sup>	B <sup>i</sup>
Triphenylphosphine	96	67
Thiourea	92	74
Sodium thiosulfate <sup>ii</sup>	98	68
Sodium azide	78	70

i: A, in DMF, 2 h; B, in dioxane, 3 h.

ii: one drop of water added to the reaction medium.

#### REFERENCES

1. T.-L. Ho, Synthesis, in press.

Received: January 16, 1973