

THE DEMETHYLATION OF QUARTERNARY AMMONIUM SALTS OF SOME ALKALOIDS
BY SODIUM SELENOPHENOLATE

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A short time back (1), a new method of demethylation of quarternary ammonium salts by means of sodium thiophenolate was described. Recently (2), demethylation was also carried out by using sodium salt of p-methylthiophenol. Furthermore, sodium salt of thiophenol was made use of (3) for the N-debenzylation of some quarternary ammonium salts.

These findings prompted us to carry out demethylation of quarternary ammonium salts by application of sodium selenophenolate (this substance was prepared by heating at reflux a solution of selenophenol in toluene after addition of sodium). We expected that on using this substance the reaction rate would be faster in comparison with that of the thio-analogue.

We have attempted to demethylate six quarternary ammonium salts of different types of alkaloids with sodium selenophenolate. With some of these substances, demethylation with sodium thiophenolate was carried out simultaneously under comparable experimental conditions. In all the cases the rate of demethylation was followed by thin-layer chromatography.

All the demethylations were carried out in the following manner: To the methochloride of the alkaloid (0.5 mmol) in ethanol (10 ml) a solution of sodium selenophenolate (1 mmol) in ethanol (10 ml) was added. The mixture was stirred at room temperature for 20 min and evaporated to dryness in vacuo. The residue was taken up in 2-butanone (40 ml) and the resulting solution was heated at reflux under nitrogen. Samples of the mixture were collected at 10 min intervals and subjected to thin-layer chromatography on silica gel G. After

the reaction was completed, the reaction mixture was treated according to (1).

Table I shows that N-demethylation with sodium selenophenolate proceeds very easily in alkaloids whose nitrogen atom is present in one ring only. Alkaloids whose nitrogen atom forms part of two rings of the bicyclic system are demethylated either at a much slower rate or they are not demethylated at all (seneciphylline methochloride), which probably depends upon the steric conditions in the molecule. Demethylation did not take place in papaverine methochloride whose nitrogen atom is present in the conjugated isoquinoline system.

Table I

N-Demethylation of some methochlorides of alkaloids

Methochlorides of alkaloids	Reaction period (hr) and yields of the crystalline tertiary amine on application of:		
	Na-selenophenolate	Na-thiophenolate	
		this paper	lit. (1)
3-Ethylmorphine	2 (74%)	2 (60%)	36 (70%)
(+)-Laudanosine	2 (77%)	2 (13%)	36 (85%)
(+)-Canadine	25 (73%)		36 (75%)
(+)-1-Methoxycanadine	25 (68%)	36 (75%)	
Seneciphylline	36 (0%)		
Papaverine	36 (0%)		

The first four substances (Table I) were demethylated quantitatively according to thin-layer chromatography (a small quantity of the Hofmann degradation product was observed in (+)-laudanosine); the yields of the isolated products varied according to the ease of crystallization.

The results show the dependence of the demethylation rate upon the structure of the quarternary salts and they confirm the assumption that on using selenophenolate the reaction rate is faster.

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