Synthesis and Reaction of *N*-Methyl-*N*-tosylpyrrolidinium Perchlorate, a Selective Tosylating Reagent

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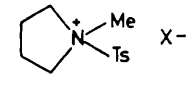
Summary Reaction of *N*-methylpyrrolidine and tosyl chloride in the presence of $AgClO_4$ afforded *N*-methyl-*N*-tosylpyrrolidinium perchlorate (II) as a stable, crystalline salt, which can be used for the selective tosylation of an amino-group in the presence of a hydroxy-group.

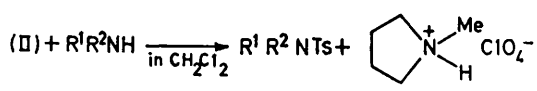
WE reported previously that methylation of *NN*-disubstituted sulphonamides took place on nitrogen rather than on oxygen[1] and the resulting sulphonamidium salts similar to (I) were hydrolysed readily by dilute HCl giving methylamine derivatives, which in turn suggested that they could be used as an effective tosylating reagent. We have found that *N*-methyl-*N*-tosylpyrrolidinium perchlorate (II) can be used as a selective tosylating reagent.

Some aliphatic amines can be tosylated by $TsMe_3N^+$-$SbCl_6^-$ in fair yield but usually a considerable amount of tosyl chloride is produced in place of the expected sulphonamides, presumably by attack of Cl^- liberated from $SbCl_6^-$ on the sulphur atom. This side reaction was avoided by use of ClO_4^- as counteranion. The sulphonamidium per-



(I) X = $SbCl_6^-$
(II) X = ClO_4^-

chlorate (II),† m.p. 148—150°, was prepared (67·7% yield) by tosylation of *N*-methylpyrrolidine with tosyl chloride in the presence of silver perchlorate[2] in the dark.



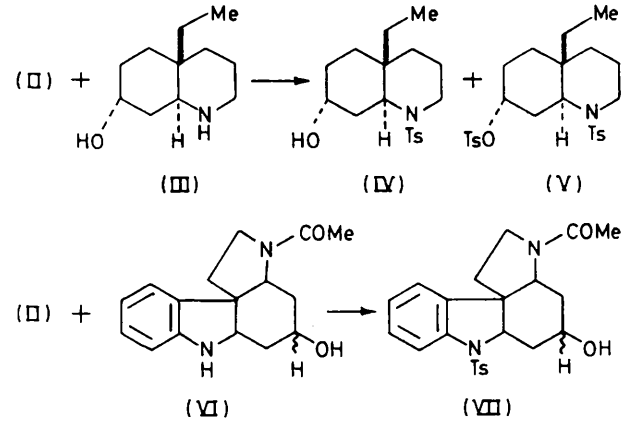
SCHEME 1

Tosylation of primary and secondary amines with 1 mol. equiv. of (II) proceeded smoothly as expected, and even sterically hindered dicyclohexylamine gave a much better yield at 0 °C than those reported.[3] With the weakly basic diphenylamine, however, the reaction was slow and required forcing conditions.

TABLE. *Tosylation of amines with reagent* (II)

Amine	Conditions	Yield (%) of sulphonamide
p-Toluidine	0°; 1·5 h	97·8
Indoline	0°; 2 h	96·7
Dicyclohexylamine	0°:1·5 h	65·8
Dicyclohexylamine	0°; 1·5 h, then 12°; 1 h	65·8
Diphenylamine	40°; 2 h	49·8

This reagent is significant in its inertness towards a hydroxy-group. For example, cholesterol was recovered unchanged after it had been stirred for 7 h at room temperature with (II) in CH_2Cl_2. We assumed that only nitrogen would be tosylated if both amino- and hydroxy-groups were present in the substrate. In practice, the bicyclic amino-alcohol (III)[4] afforded the *N*-tosyl derivative (IV) in 80% yield together with the *ON*-ditosyl derivative (V) in only 5% yield. Further, the tetracyclic amino-alcohol (VI),[5] an intermediate in the synthesis of $\beta\beta$-disubstituted indoline alkaloids, gave the *N*-tosyl derivative (VII) (75%). *N*-Tosylation of (VI) has been carried out repeatedly in this laboratory using the TsCl–10% NaOH system but yields were unusually unsatisfactory (20—40%).



SCHEME 2

Reagent (II) is reasonably stable in water (*ca.* 50% unchanged after 60 min), which shows that (II) may be applicable to protein modification.

We thank Mr. J. Shimizu for tosylation of the amino-alcohol (VI).

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† Satisfactory elemental analysis was obtained for (II) and its spectral data were comparable to those of (I). Compound (II) can be stored for at least six months without significant decomposition.

[1] T. Oishi, K. Kamata, and Y. Ban, *Chem. Comm.*, 1970, 777.
[2] F. Klages and K. Hoheisel, *Chem. Ber.*, 1963, **96**, 2057; F. Klages and F. E. Malecki, *Annalen*, 1966, **691**, 15.
[3] It has been reported that dicyclohexylamine was tosylated by $TsCl^+$ α-picoline in 7% yield and by $TsCl^+$ 10% NaOH in 20% yield (D. Klamann and H. Bertsch, *Chem. Ber.*, 1956, **89**, 2007).
[4] Y. Ban, Y. Sato, I. Inoue, M. Nagai, T. Oishi, M. Terashima, O. Yonemetsu, and Y. Kanaoka, *Tetrahedron Letters*, 1965, 2261.
[5] The synthesis of (VI) will be published elsewhere.