

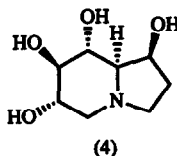
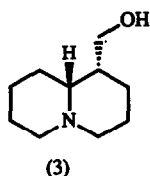
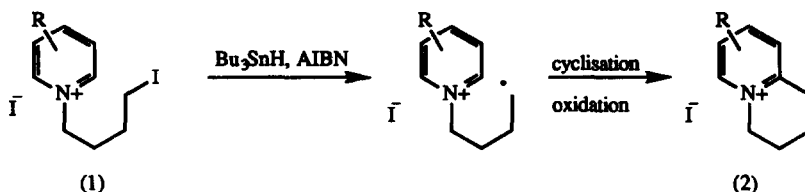
## Intramolecular Free-Radical Substitution Reactions of Pyridinium Rings: Efficient Formation of [5,6]- and [6,7]-Fused Ring Systems.

John A. Murphy\* and Michael S. Sherburn,

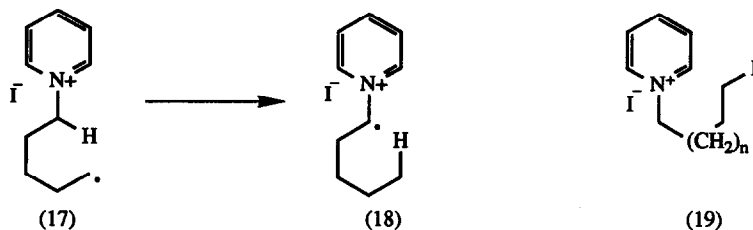
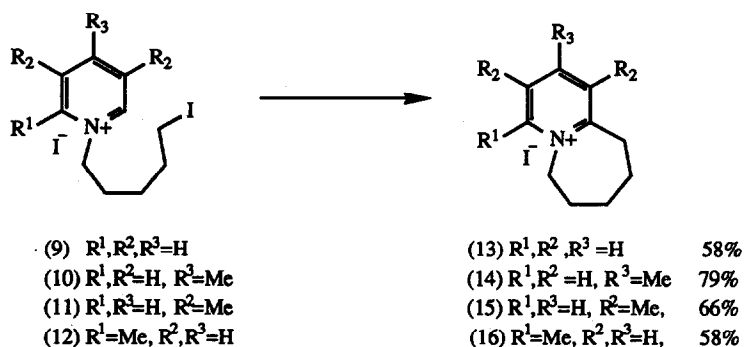
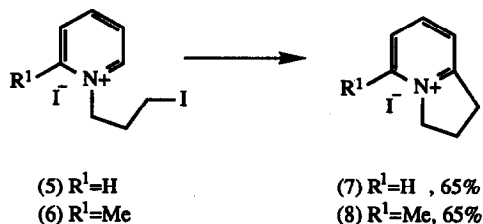
Department of Chemistry, University of Nottingham, University Park, Nottingham NG7 2RD.

The scope of intramolecular radical-induced substitution of pyridinium salts has been investigated, and it has been shown that [5,6] and [6,7]-membered fused ring systems form with surprising efficiency.

We have recently reported<sup>1</sup> the intramolecular addition of free-radicals formed from (1), and the isolation of bicyclic tetrahydroquinolizinium salts (2) using mild tributylstannyl radicals to effect the reaction.



The formation of the tetrahydroquinolizinium salts may prove to be a very useful extension to methods for forming quinolizidine alkaloids such as lupinine (3), but we were interested in investigating whether this type of reaction could be used to synthesise a broader range of fused-ring products, including the indolizidine ring system of important alkaloids like castanospermine (4). This paper describes our results. To test for formation of [5,6] fused systems the substrates (5) and (6) were synthesised. The conversions to (7) and (8) can be viewed as involving unfavourable *5-endo-trig* cyclisations<sup>3,4</sup>. However, by reacting (5) and (6) with tributyltin hydride (1.3 equivalents) and AIBN (1.2 equivalents) in a mixture of acetonitrile and tetrahydrofuran as solvent, smooth transformation to the bicyclic products occurred in the yields shown. Extending the reaction to the formation of 7-membered rings was also successful. Examples (9) to (12) gave the bicyclic products (13) to (16) as the sole isolable products. To ensure optimum yield, two equivalents of AIBN were required. The clean formation of these products demonstrates that the potentially competing process (17)  $\rightarrow$  (18)<sup>5</sup> in which a benzylic hydrogen is abstracted is not seen.



[Attempts to form larger rings using (19) as substrate ( $n=3$  or  $7$ ) were not successful]. These reactions are particularly gratifying because the use of the lipophilic tributyltin hydride as radical source leads to extremely facile product isolation **requiring no chromatography**. The aromatic products do not suffer the problems of polysubstitution seen in the intermolecular reactions of pyridinium salts reported by Minisci and co-workers<sup>2</sup>. The intramolecular substitution reactions reported here therefore have significant scope for the synthesis of alkaloids including indolizidines.

**Acknowledgments.** We thank the S.E.R.C. for the award of a Quota studentship.

#### References.

1. J. A. Murphy and M. S. Sherburn, *Tetrahedron Letters*, in press.
2. F. Minisci, E. Vismara and F. Fontana, *Heterocycles*, **1989**, *28*, 489.
3. J. E. Baldwin, *J. Chem. Soc., Chem. Commun.* **1976**, 734.
4. A. L. J. Beckwith, *Tetrahedron*, **1981**, *37*, 3073.
5. C. A. Grob and H. Kammüller, *Helv. Chim. Acta*, **1957**, *40*, 2139.