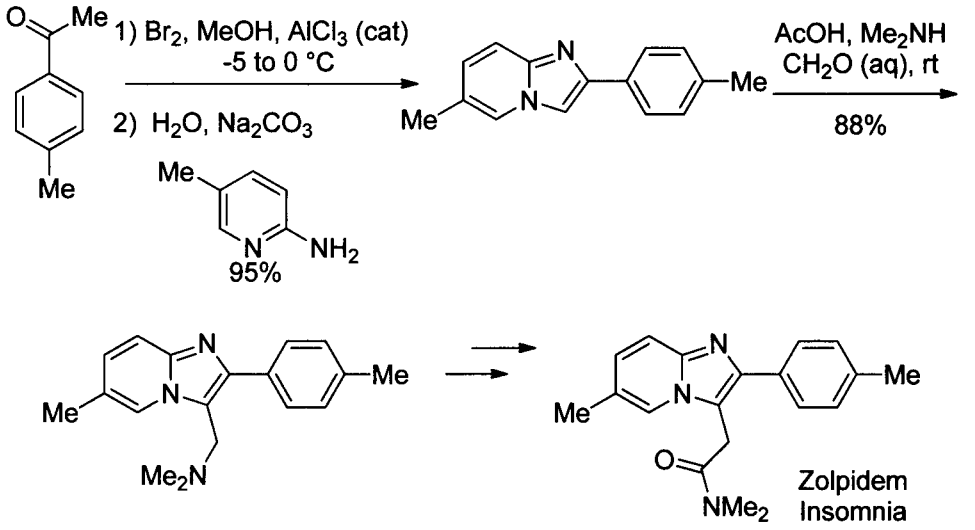
Another pharmaceutically important fused-imidazole ring system is the popular sleeping aid medication zolpidem. Bromination of 4-methylacetophenone and condensation with methylated 2-amino pyridine provides the fused-imidazole in good overall yield. Note that the ring nitrogen on the aminopyridine reaction reacts with the bromide carbon. Mannich-type alkylation at the unsubstituted 5-position provides the dimethylaminomethyl substituent in good yield. Further elaboration yields zolpidem.[32]



8.3.9 Miscellaneous Imidazole Ring Construction

Imidazole synthesis utilizing 2-aminopyridines as amine source

The use of microwave has recently been used to provide 5-amino-imidazoles from 2-aminopyridines. At a higher temperature and longer reaction times, dehydration occurs to form the imidazo-pyridinium salts. Reaction with hydrazine adds to the pyrimidinium salt, which then undergoes rearrangement to open the ring. The unstabilized diene undergoes hydrolysis to provide the 2-amino-4,5-di-substituted 1*H*-imidazole. Chemically, PPA can be used to form the pyrimidinium salt also.[33,34]