Method for Annelation of Pyridinium Rings on to Nitrogen Heterocycles

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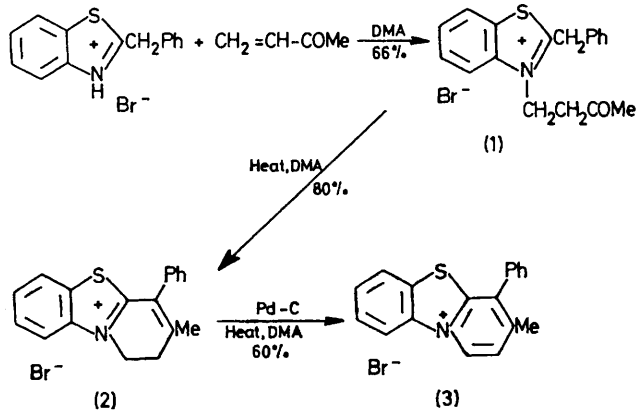
Summary Protonated heterocycles possessing an alkyl substituent on the carbon atom adjacent to the positive nitrogen react with methyl vinyl ketone to form adducts which can be converted into fused pyridinium salts.

WE report a novel synthesis of fused pyridinium salts by the reaction of protonated heterocycles with methyl vinyl ketone (MVK). The general reaction scheme is shown for 2-benzylbenzothiazolium bromide.†

Compound (**1**) was synthesised from 2-benzylbenzothiazolium bromide and MVK at room temperature in *e.g.*, MeCN or dimethylacetamide (DMA). The addition of MVK to pyridinium chloride[1] and 3,4-dihydroisoquinolinium perchlorate[2] has been described previously. Heating the

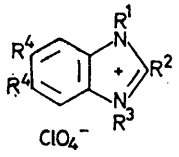
† All new compounds gave satisfactory elemental analyses and had spectral properties in agreement with the assigned structures.

adduct (**1**) in DMA brought about ring closure to the dihydropyridinium salt (**2**), which was readily converted into the corresponding pyridinium salt (**3**) by heating with Pd–C.



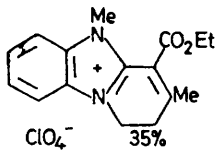
Similar results were obtained with 2-benzyl-5-phenylbenzoxazolium and 2-benzyl-1-ethylimidazo[4,5-*b*]quinoxalinium salts. Starting from the corresponding 2-methylbenzothiazolium adduct an analogous series of transformations was carried out but the yield in the cyclisation step was much lower (*ca.* 10% yield) because of the reduced acidity of the 2-alkyl group, thereby allowing the loss of MVK by a reverse Michael reaction to compete with ring closure.

With the benzimidazolium adduct (**4**), despite the activating effect of the phenyl group, the benzylic hydrogens were not acidic enough for ring closure to compete with the reverse Michael reaction. Therefore, the 2-ethoxycarbonylmethylbenzimidazolium perchlorate (**5**) was prepared to increase the acidity of the methylene group. However, the reaction of MVK with (**5**) gave a mixture of uncharacterised adducts which was cyclised to the products (**6**) and (**7**) by heating in pyridine. The mixture apparently arose from both nitrogen and carbon addition to the double bond of MVK. As with the benzothiazole example (**2**), compound (**6**) was aromatised in 54% yield by heating with Pd–C in DMA.

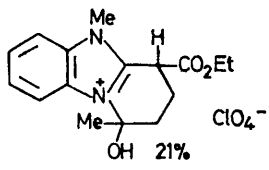


(4) R^1 = Et, R^2 = CH_2Ph, R^3 = CH_2CH_2COMe, R^4 = Cl

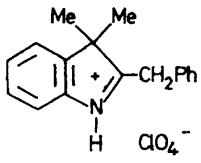
(5) R^1 = Me, R^2 = CH_2CO_2Et, R^3 = H, R^4 = H



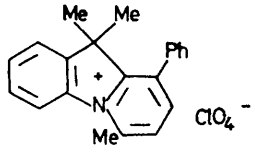
(6)



(7)



(8)



(9)

With the indolium perchlorate (**8**), in which the methylene group is more acidic than in the corresponding benzothiazolium salt, the product isolated was that of exclusive addition of the benzylic carbon to the MVK. Also, spontaneous cyclisation and aromatisation occurred to form the pyrido[1,2-*a*]indolium salt (**9**) in 40% yield.

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[1] J. P. Stevens and Co. Inc., Fr.P. 1,349,141/1964 (*Chem. Abs.* 1964, **61**, 10837c).

[2] Magyar Tudomanyos Akademia, B.P. 958,936/1964 (*Chem. Abs.* 1965, **62**, 11790); C. Szantay and J. Rohaly, *Chem. Ber.*, 1965, **98**, 557.