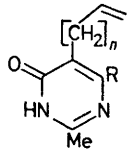
New Route to Annulated Pyridines and Pyrimidines

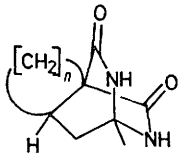
By Lyn B. Davies, Peter G. Sammes,* and Robert A. Watt
(*Department of Chemistry, The City University, St. John Street, London* EC1V 4PB)

Summary The title compounds can be obtained by bridge elimination of the primary intramolecular cycloadducts between pyrimidines and multiple bonds.

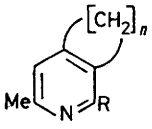
INTRAMOLECULAR cycloadditions between olefins and 4-hydroxy-6-oxopyrimidines such as (**1**) and (**2**) are known to lead to relatively stable bicyclic adducts (**3**) and (**4**), respectively.[1] By suitable variations of the substitution pattern around the heterocyclic ring, products arising from the sequential elimination of one of the bridges of the intermediate cycloadduct can also be observed. Herein we report some examples which lead to the formation of annulated heterocyclic systems. Although some related bridge eliminations have been observed with pyrazine[2] and pyrimidine[3] adducts, these resulted from inter- rather than intra-molecular reactions.



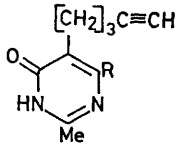
(1); n = 3, R = OH
(2); n = 4, R = OH
(5); n = 3, R = Me
(6); n = 3, R = Ph
(10); n = 4, R = Me



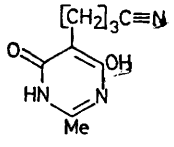
(3); n = 3
(4); n = 4



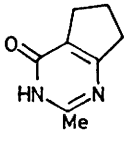
(7); n = 3, R = Me
(8); n = 3, R = Ph
(11); n = 4, R = Me



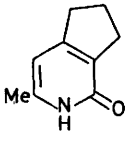
(9); R = Me
(14); R = OH



(12)



(13)



(15)

Thermolysis of the mono-oxopyrimidines (**5**) and (**6**), in either acetonitrile or dimethylformamide, at 180—200 °C afforded, as the major products, the annulated pyridines (**7**) (65%) and (**8**) (51%).† Spectral monitoring of the reactions did not reveal any appreciable quantities of the expected intermediate bicyclic adducts, hence the subsequent elimination of one mole of cyanic acid must be at least as fast as the initial cyclisation. The observed products must arise *via* oxidation of the dihydroaromatic systems produced as a result of the retro-Diels–Alder process. Indeed, mass spectral examination of the crude product showed that traces of such dihydro-species were present. Under the conditions of the reaction, however, dehydrogenation to the observed pyridine products occurs quite efficiently. As expected, use of the acetylene derivative (**9**) afforded the pyridine (**7**) directly at 180 °C and in good yield (60%).

The reaction is not restricted to the formation of cyclopentanopyridines, since use of the homologous starting material (**10**) afforded the cyclohexanopyridine (**11**).

Isolated nitrile groups, whilst generally unreactive towards intermolecular cycloadditions, have recently been shown to participate when incorporated into an intramolecular reaction.[4] Thus, on heating at 200 °C, the nitrile (**12**) was smoothly converted into the corresponding annulated pyrimidine (**13**), m.p. 205—207 °C.

One further example of these addition–elimination reaction sequences is of note. Although the cycloadducts of types (**3**) and (**4**) are relatively stable, the corresponding cycloadducts from the acetylene derivatives undergo bridge elimination of one mole of cyanic acid. Thus the pyrimidine derivative (**14**) [*cf.* (**1**)] reacts smoothly on heating to produce the annulated pyridone (**15**), m.p. 160—161 °C.

These examples illustrate the synthetic utility and versatility of the intramolecular mode of cycloaddition.

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† All compounds have been characterised by microanalysis and/or mass spectral identification.

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