A New Synthesis of N-Bridgehead Heterocycles

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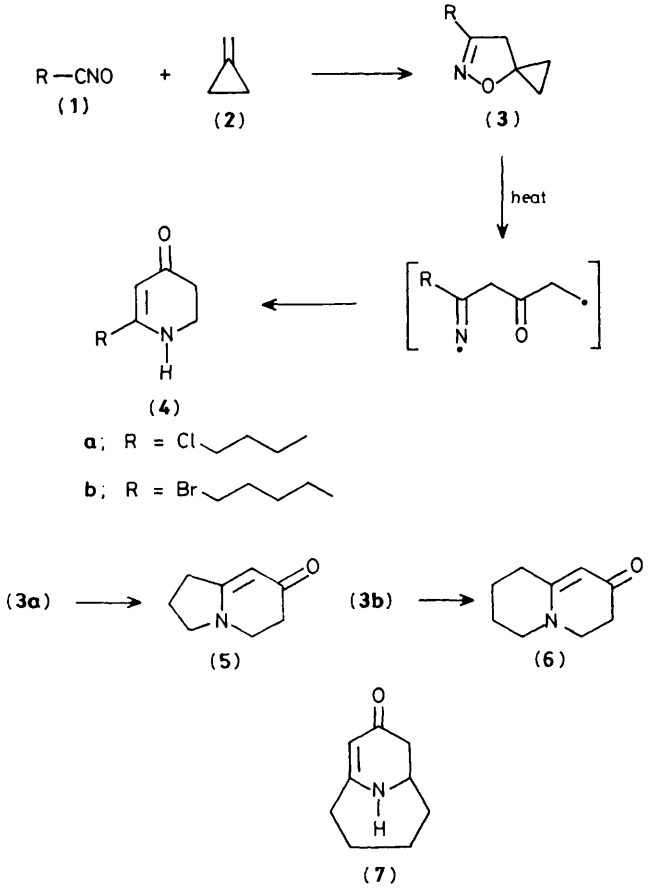
Indolizine and quinolizine derivatives are obtained by rearrangement of 4,5-dihydroisoxazole-5-spirocyclopropanes with a side chain in position 3 suitable for ring-closure.

Bicyclic heterocycles of the indolizine and quinolizine series, having a bridgehead N atom, are of interest because of their occurrence in many alkaloid families,[1] and their synthesis provides an important challenge.

The rearrangement of 4,5-dihydroisoxazole-5-spirocyclopropane derivatives (**3**) to 5,6-dihydro-4-pyridone derivatives (**4**) reported recently[2] prompted us to employ this reaction for a simple preparation of indolizine and quinolizine derivatives. The intermediate spiranes (**3a**,**b**) were obtained [yields: (**3a**) 52%; (**3b**) 46%] by cycloaddition of methylenecyclopropane (**2**) to the appropriate nitrile oxides (**1a**,**b**), prepared *in situ* from ω-halogenonitroalkanes by Mukaiyama's method;[3] the reactions appeared to be completely regioselective. On thermolysis of the intermediates (**3a**) and (**3b**), the corresponding dihydropyridones (**4**) were not detected, as ring-closure occurred immediately to 2,3,5,6-tetrahydro-(1*H*)-indolizin-7-one (**5**)[4] and 3,4,6,7,8,9-hexahydro-(2*H*)-quinolizin-2-one (**6**),[5] respectively. These rearrangements were



carried out in boiling dimethylformamide (0.05 M solution) over solid potassium carbonate [yields: (**5**) 60%; (**6**) 40%].† On flash vacuum pyrolysis of the intermediates (**3a**) and (**3b**) at 400 °C, the products (**5**) and (**6**) were isolated as their hydrohalide salts. The corresponding free bases were obtained by treatment with sodium methoxide in methanol; the isomer (**7**) of the quinolizinone (**6**) was not detected in this case.

The products (**5**) and (**6**) have been prepared previously in connection with studies on Elaeocarpus alkaloids (**5**)[4] and Lupine alkaloids (**6**)[5] by much longer procedures. The present method is clearly much better.

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† Beside (**6**), an isomer was isolated (30% yield), whose spectra are in agreement with the structure (**7**). This product might arise from either intermediate (**4b**) or its open-chain precursor.