A SYNTHETIC ROUTE TO THE MORPHAN RING SYSTEM FROM NORBORNADIENE. THE SYNTHESIS OF THE 6,7-PYRIDAZINOANNELATED MORPHAN

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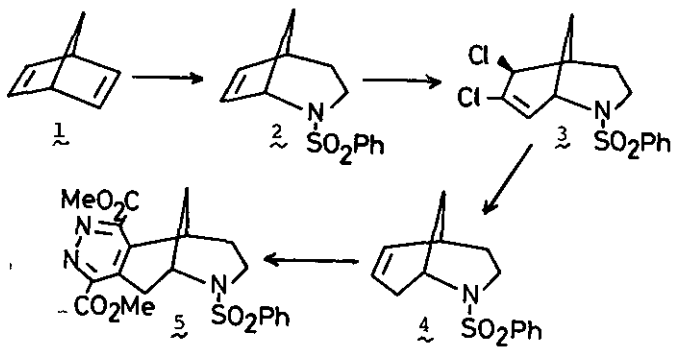
A general synthetic route to the morphan ring system starting from readily available norbornadiene 1 has been developed. The diene 1 was converted into azabicyclic monoene 2 by the reaction of the diene 1 with benzenesulfonyl azide to give 2-phenylsulfonyl-2-azabicyclo[3.2.1]octa-3,6-diene by thermal isomerization, followed by the reduction of the azabicyclic diene with lithium aluminium hydride and the protection of the -NH- group with benzenesulfonyl chloride. The ring expansion of the monoene 2 to the morphan ring system was achieved successfully by the cheletropic addition of dichlorocarbene to 2, using a phase-transfer technique, followed by the thermal isomerization of the adduct to give the monoene 3 (54%) together with its positional isomer (43%). The positional isomer was converted into 3 in 65% yield by treatment with lithium chloride in DMF at 50°C for 7h. The conversion of the monoene 3 to 4 was achieved by the reductive cleavage of the C_6-Cl and N-S bonds of 3 with lithium aluminium hydride, the reduction of the C_7-Cl bond with sodium in liquid ammonia and the protection of the -NH- group with benzenesulfonyl chloride. The fusion of a pyridazine ring onto the 6,7-position of the morphan ring was carried out by the Diels-Alder reaction of the monoene 4 with 3,6-dimethoxycarbonyl-1,2,4,5-tetrazine (1 : 2 molar ratio). The reaction proceeded by the evolution of nitrogen and the dehydrogenation of the adduct with tetrazine to give the 6,7-pyridazinoannelated morphan 5 in a quantitative yield.



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