SYNTHESIS OF MORPHAN DERIVATIVES FROM NORBORNADIENE BY SKELETAL TRANSFORMATION

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Since it is now appreciated that some morphan derivatives such as pentazocine and its analogues have significant analgesic properties, it is worthwhile to develop a new method for building morphan skeleton, widely applicable to new structural variants. Herein, we wish to describe a new approach for preparing morphan derivatives from norbornadiene by skeletal transformation, which involves thermal rearrangement of unsaturated tricyclic aziridines and adducts of dichlorocarbene, accompanied by ring expansion. The structure of all compounds obtained here was determined by elemental analysis and IR, NMR, and MS spectra.

Norbornadiene was converted into 2-benzenesulfonyl-2-azabicyclo[3.2.1]oct-3,6-diene in 86% yield. This reaction proceeded via the thermal rearrangement of 3-benzenesulfonyl-3-azatricyclo[3.2.1.$0^{2,4exo}$]oct-6-ene formed by the decomposition of an adduct in the 1,3-dipolar addition of benzenesulfonyl azide to norbornadiene. The diene compound obtained was reduced selectively with lithium aluminium hydride to 2-azabicyclo[3.2.1]oct-6-ene (73%) which was converted into 2-benzenesulfonyl-2-azabicyclo[3.2.1]-oct-6-ene in 71% yield by the reaction with benzenesulfonyl chloride using a phase-transfer technique. The catalytic hydrogenation of the diene compound over 5% Pd-C catalyst and its reduction with di-imide resulted in selective reduction of the C_6–C_7 double bond.

The expansion of the ring involving the C_6–C_7 double bond was achieved by the addition of dichlorocarbene to 2-benzenesulfonyl-2-azabicyclo[3.2.1]oct-6-ene (51%), followed by the thermal rearrangement of the adduct to afford 2-benzenesulfonyl-6,7- or 7,8-dichloro-2-azabicyclo[3.3.1]non-7- or 6-ene in 63 and 36% yields respectively. The thermal rearrangement was carried out by heating at 130–135°C without solvent. The treatment of two isomers with lithium aluminium hydride and then sodium in liquid ammonia afforded 2-azabicyclo[3.3.1]non-6- and 7-ene (41 and 62%). Two monoene compounds obtained were converted into 2-(3-methyl-2-butenyl)- and benzyl-2-azabicyclo-[3.3.1]non-6-ene and their 7-ene isomers by alkylation with 1-bromo-3-methyl-2-butene and benzyl bromide in good yields. The above sequence provides a new route to morphan analogues.