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A SYNTHESIS OF FUSED-RING CYCLOHEPTANOLS VIA CYCLIZATION OF UNSATURATED ALDEHYDES

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Recent work has clearly shown the utility of cation-initiated olefin cyclizations for the synthesis of cyclohexane[1] and cyclopentane[2] derivatives. Our interest in hydroazulenes and related fused-ring cycloheptane derivatives prompted us to examine the possibility of using such reactions for closing seven membered carbocyclic rings. Preliminary studies have now demonstrated the feasibility of this approach and have yielded results of both practical and theoretical interest which we wish to report at this time.

The first system examined, unsaturated aldehyde 3, was prepared from the previously reported ketone 1[3] whose oxime derivative underwent fragmentation upon treatment with p-toluenesulfonyl chloride in pyridine at reflux.[4] The resulting unsaturated nitrile 2 [λ_{max}^{film} 3.26 (HC=C), 4.46 (CN), 6.08 (C=C), 7.25, and 11.2 μ ($C=CH_2$)] was reduced at -30° by lithium triethoxyaluminohydride[5] giving the desired aldehyde 3 [λ_{max}^{film} 3.26 (HC=C), 3.68 (aldehyde CH), 5.79 (CO), 6.08 (C=C), 7.25, and 11.2 μ ($C=CH_2$)]. Cyclization was effected by brief treatment of this substance with stannic chloride in benzene[6] whereupon it was nearly quantitatively converted to the bicyclo[5.4.0]undecanol 4 [λ_{max}^{film} 2.96 (OH), 3.26 (HC=C), 6.08 (C=C), 9.84, and 11.2 μ ($C=CH_2$); $\delta_{TMS}^{CCl_4}$ 4.89 ($C=CH_2$; complex pattern, $\Delta\nu \sim 4$ Hz), 3.89 (H-4; $J_{4,3} = 5.0$, $J_{4,3'} = 7.0$, $J_{4,5} + J_{4,5'} = 10.4$ Hz), 2.97 (OH), 2.39 (H-3, H-3'; $J_{3,3'} = -13.0$, $J_{3,4} = 5.0$, $J_{3',4} = 7.0$ Hz; $\Delta\nu_{3,3'} = 28.7$ Hz), and 0.89 ppm (C-6 CH_3; doublet, J = 6.1 Hz).[7]

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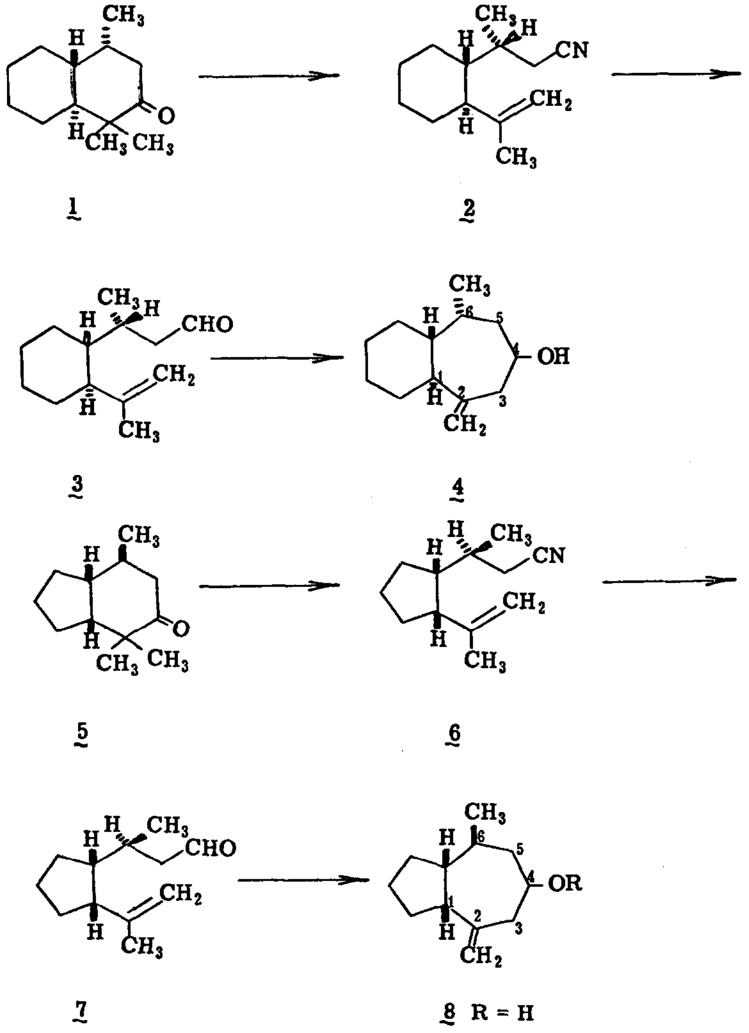

1 2 3 4 5 6 7

8 R = H

9 R = Ac

Similarly the trimethylhydrindanone **5**, prepared along the lines previously reported for decalone **1**,[3] was converted as described above to nitrile **6** [λ_{max}^{film} 3.26 (HC=C), 4.46 (CN), 6.09 (C=C), 7.24, and 11.2 μ ($C=CH_2$)] and aldehyde **7** [λ_{max}^{film} 3.25 (HC=C), 3.68 (aldehyde C-H), 5.79 (CO), 6.09 (C=C), 7.25, and 11.2 μ ($C=CH_2$)]. Exposure to stannic chloride in benzene converted this aldehyde in nearly quantitative yield to the bicyclo[5.3.0]decanol **8** [λ_{max}^{film} 2.97 (OH), 3.26 (HC=C), 6.10 (C=C), 9.61, 9.73-9.83, and 11.2 μ ($C=CH_2$); $\delta_{TMS}^{CCl_4}$ 4.90 ($C=CH_2$, $W_{h/2} = 3.0$ Hz), 3.95 (H-4, broad complex pattern), 2.41 (OH), 2.36 (H-3, H-3' obscured by other resonance peaks; $J_{3,4} \sim 4$, $J_{3',4} \sim 6$ Hz; $\Delta\nu_{3,3'} \sim 7$ Hz), 0.95 ppm (C-6 CH_3, unresolved)]. The acetate derivative **9** displayed in its nmr spectrum a more nearly first-order pattern for the allylic protons[7]: $\delta_{TMS}^{CCl_4}$ 5.10 (H-4; $J_{4,3} = 6.1$, $J_{4,3'} = 4.5$, $J_{4,5} + J_{4,5'} = 9.4$ Hz), 4.89 ($C=CH_2$), 2.79 (H-1, broad unresolved pattern), 2.51 (H-3, H-3'; $J_{3,4} = 6.1$, $J_{3',4} = 4.5$, $J_{3,3'} = -13.6$ Hz; $\Delta\nu_{3,3'} = 8.2$ Hz), 2.06 (CH_3CO), and 1.03 ppm (C-6 CH_3, unresolved).

The spectra of bicyclic alcohols **4** and **8** and of acetate **9** fully support the assigned structures. The gas chromatograms of these materials show essentially one peak on a number of columns under a variety of conditions. Thus the cyclizations of unsaturated aldehydes **3** and **7** lead not only to a great predominance of the respective exocyclic methylene isomers, but also appear to give a great predominance of one alcohol epimer. Since these bicyclic olefins isomerize upon prolonged exposure to the cyclization reaction conditions, their initial preference for the exocyclic position must be a kinetic rather than a thermodynamic result. Assuming a concerted or nearly concerted cyclization mechanism, the more facile loss of a methyl vs methine proton from the unsaturated aldehydes **3** and **7** can be readily understood in stereoelectronic terms. Thus whereas the allylic methine C-H bond of these aldehydes will be very nearly coplanar with the isopropenyl double bond in conformers leading to energetically feasible transition states, the relatively free rotation of the vinyl methyl group will enable one of the methyl protons to easily attain a perpendecular orientation to this double bond whereby it can be readily lost in a concerted reaction.[8]

We are currently investigating the relative configuration of C-4 in the bicyclic alcohols **4** and **8**.

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