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ON THE STEREOSPECIFICITY OF THE REARRANGEMENT OF SPIRO[3-HYDROXYPIPERIDINE-4,2′-OXIRANES] BY THE ACTION OF METHYLMAGNESIUM IODIDE

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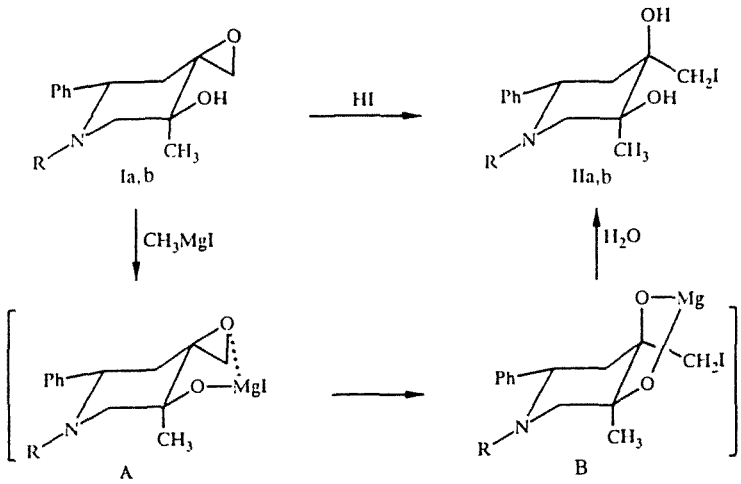
We have previously reported [1] that spiro[3*a*-hydroxypiperidine-4,2′-oxiranes] undergo a rearrangement into 3-acetyl-3-hydroxymethylpyrrolidines by the action of organomagnesium compounds [2]. Since this transformation was observed for the first time, it was of interest to study its stereochemical features, and in particular, the influence of the configuration of the carbinol center of the piperidine ring on the course of the reaction. For this purpose we studied the reaction of spiro[3*e*-hydroxypiperidin 4,2′-oxiranes] (Ia, b) with methylmagnesium iodide.



I, II a R = CH_3, b R = $PhCH_2$

It was found that the change of the configuration at $C_{(3)}$ to the opposite one directs the reaction into an entirely different path. The corresponding iodohydrins (IIa, b) are formed as the only reaction products, the structure of which was confirmed by means of PMR, as well as by a countersynthesis — the reaction of oxiranes Ia, b with hydriodic acid. It is probable that a chelate complex A is formed at the first stage by the action of the organomagnesium compound on epoxide I. The subsequent intramolecular attack of iodine on the epoxide ring activated by the chelate formation leads to alcoholate B, which on hydrolysis converts into iodohydrin II. A similar complex cannot be formed in the case of spiro[3*a*-hydroxypiperidine-4,2′-oxiranes] because of the trans-diaxial disposition of the hydroxy group in the 3-position and the oxygen in the epoxy ring. Thus, the rearrangement with the ring contraction by the action of the Grignard reagent is characteristic only for spiro[3*a*-hydroxypiperidine-4,2′-oxiranes] but not for their epimers at $C_{(3)}$.

3,4-Dihydroxy-1,3-dimethyl-4-iodomethyl-6-phenylpiperidine (IIa, $C_{14}H_{20}INO_2$), yield 74%, mp 109-110°C. PMR spectrum ($CDCl_3$): 1.51 (3H, s, 3-CH_3); 1.62 (1H, dd, J = 14.2 and 11.6 Hz, 5-Ha); 2.00 (3H, s, N-CH_3); 2.02 (1H, dd, J = 14.2 and 3.5 Hz, 5-H_e); 2.33 (1H, s, OH); 2.48 (1H, s, OH); 2.62 (1H, d, J = 10.7 Hz, 2-H_a); 2.63 (1H, d, J = 10.7 Hz, 2-H_e); 3.20 (1H, dd, J = 11.6 and 3.5 Hz, 6-H_a); 3.35 (1H, d, J = 10.1 Hz, CH_2I); 3.78 (1H, d, J = 10.1 Hz, CH_2I); 7.30 (5H, m, H_{ph}).

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1-Benzyl-3,4-dihydroxy-4-iodomethyl-3-methyl-6-phenylpiperidine (IIb, $C_{20}H_{24}INO_2$), yield 82%, mp 224-225°C (dec.). PMR spectrum ($CDCl_3$): 1.42 (3H, s, 3-CH_3); 1.66 (1H, dd, J = 14.3 and 11.4 Hz, 5-H_a); 2.08 (1H, dd, J = 14.3 and 3.5 Hz, 5-H_e); 2.34 (1H, s, OH); 2.44 (1H, d, J = 11.0 Hz, 2-H_a); 2.53 (1H, d, H = 11.0 Hz, 2-H_e); 2.81 (1H, d, J = 13.6 Hz, $PhCH_2$); 3.32 (1H, d, J = 10.5 Hz, CH_2I); 3.52 (1H, dd, J = 11.4 and 3.5 Hz, 6-H_a); 3.72 (1H, d, J = 10.5 Hz, CH_2I); 3.74 (1H, d, J = 13.6 Hz, $PHCH_2$); 7.25 (10H, m, H_{ph}).

The results of the analysis of compounds IIa,b correspond to the calculated values.

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