TOTAL SYNTHESIS OF 5,6,7,8-TETRAHYDROQUINOLINES AND QUINOLINES

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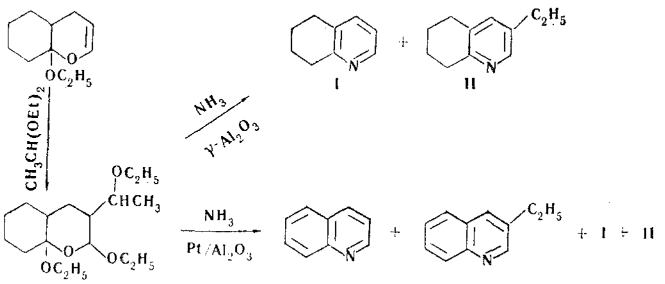
The condensation of 2-ethoxy-2,3-tetramethylene-3,4-dihydro-1,2-pyran with acetal and ethyl orthoformate was studied. The condensation products react with ammonia on γ-aluminum oxide to form the corresponding tetrahydroquinolines; a mixture of tetrahydroquinolines and quinolines is formed from these condensation products on platinized γ-aluminum oxide.

It has previously been demonstrated that various 3-substituted pyridines can be obtained from the products of the condensation of 2-ethoxy-3,4-dihydro-1,2-pyrans with acetals [1-4]. We have studied the reaction of 2-ethoxy-2,3-tetramethylene-3,4-dihydro-1,2-pyran with acetal and ethyl orthoformate in the presence of boron trifluoride etherate. When the resulting ethoxy-substituted tetrahydropyrans are passed with ammonia over a catalyst (γ-Al_2O_3 or Pt/Al_2O_3), they give a mixture of unsubstituted and 3-substituted tetrahydroquinolines and quinolines.



EXPERIMENTAL

The products were analyzed with a Varian 705 gas-liquid chromatograph with a flame-ionization detector, SE-30 on Chromosorb W as the liquid phase, a column temperature of 210°C, a gas carrier (N_2) flow rate of 120 ml/min, and an attenuator setting of 1/100. The maximum sensitivity of the apparatus was 10^{-9} g. The tetrahydroquinolines and quinolines were identified by comparison of the retention times with those of known samples obtained by the method in [5].

2,6-Diethoxy-3-(1-ethoxyalkyl)-5,6-tetramethylenetetrahydropyrans (general method). Three to four drops of boron trifluoride etherate were added to 6.3 g (0.027 mole) of acetal (or ethyl orthoformate), the reaction mass was heated to 50-60°C, and 9.8 g (0.053 mole) of 2-ethoxy-2,3-tetramethylene-3,4-dihydro-1,2-pyran was added slowly with stirring from a dropping funnel. The mixture was held at 50-60°C for 1 h and was then allowed to stand overnight. It was washed with 5% potassium carbonate solution and water, dried, and distilled to give 42.2% of 2,6-diethoxy-3-(1-ethoxyethyl)-5,6-tetramethylenetetrahydropyran with bp 138-140°C (4 mm), n_D^{20} 1.4640, and d_4^{20} 0.9767 (Found: C 69.1; H 10.4%. $C_{17}H_{31}O_4$. Calculated: C 68.0; H 10.7%) and 35.1% of 2,6-diethoxy-3-diethoxymethyl-5,6-tetramethylenetetrahydropyran with bp 109-113°C (13 mm), n_D^{20} 1.4769, and d_4^{20} 0.9937 (Found: C 71.1; H 10.7%. $C_{18}H_{33}O_5$. Calculated: C 69.4; H 10.4%).

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Mixture of 5,6,7,8-Tetrahydroquinoline (I) and 3-Ethyl-5,6,7,8-tetrahydroquinoline (II). A 1.5-g (0.005 mole) sample of 2,6-diethoxy-3-(1-ethoxyethyl)-5,6-tetramethylenetetrahydropyran was passed into a flow apparatus with ammonia (tenfold excess) over a γ-Al_2O_3 catalyst at a catalytic zone temperature of 220-225° C. The catalyzate was treated with excess HCl. The nonbasic products were extracted with ether, and the aqueous solution of salts of the bases was cooled and treated with excess NaOH. The liberated bases were extracted with ether. The catalyzate contained 38.1% I and 62.0% II according to gas-liquid chromatography (GLC).

Only I (43.1%) could be identified from the reaction of 2,6-diethoxy-3-(1°-diethoxymethyl)-5,6-tetramethylenetetrahydropyran by GLC; two other compounds (13.9% and 43.0%) have retention times that do not correspond to 3-methyltetrahydroquinoline.

Mixture of Tetrahydroquinolines and Quinolines. A 1-g (0.003 mole) sample of 2,6-diethoxy-3-(1-ethoxyethyl)-5,6-tetramethylenetetrahydropyran was passed into a flow apparatus with ammonia over a Pt/Al_2O_3 catalyst as described above. The catalyzate was worked up as above, and the following composition of the reaction products was established by GLC: I (22.8%), quinoline (11.2%), II (44.5%), and 3-ethylquinoline (21.6%).

Under the same conditions, a mixture of bases, in which I (35.4%) and quinoline (1.8%) were identified by GLC, was obtained from 2,6-diethoxy-3-(1'-diethoxymethyl)-5,6-tetramethylenetetrahydropyran; two other reaction products (1.2% and 50.4%) had retention times that did not correspond to those of 3-methyltetrahydroquinoline or 3-methylquinoline.

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