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SYNTHESIS OF TETRAHYDROQUINOLINES INVOLVING REARRANGEMENT OF N-ARYLAZETIDINES AS LIKELY INTERMEDIATES+

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In view of the report[1] on the synthesis of N-arylazetidines and their rearrangement to tetrahydroquinolines, we wish to record our work on the acid catalysed cyclodehydration of 1-arylamino-3-alkanols (III) which gave the rearranged 2-substituted-1,2,3,4-tetrahydroquinolines (IV) as major or exclusive products in majority of cases instead of the expected 4-substituted-1,2,3,4-tetrahydroquinolines (V) (Table 1). The alkanols, prepared by the reduction of the corresponding ketones by interaction with sodium borohydride, were cyclodehydrated by treatment with 60-70% sulphuric acid at 98° for 10-30 minutes. In one case cyclodehydration with polyphosphoric acid (PPA) was found more convenient.

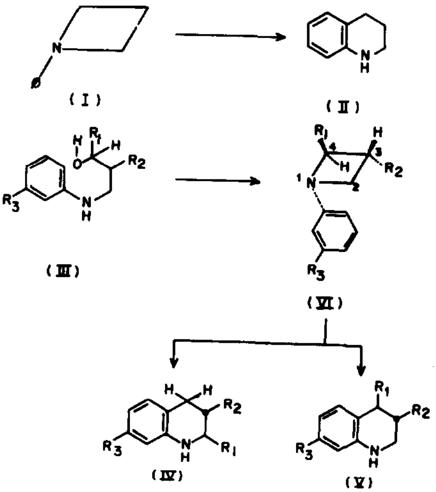

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Table 1

Starting carbinol III	Tetrahydroquinoline, IV		Tetrahydroquinoline, V		Azetidine %
	yield %	mp/bp (solvent)	yield %	mp/bp (solvent)	
R_1=C_6H_5; R_2=R_3=H.	5	Yellow oil bp, 110°/ .009 mm	50	mp, 74° (pet. ether) lit.[5], 74°	-
R_1=C_6H_5 R_2=H; R_3=OCH_3	44	mp, 143-5° (methanol)	-	-	18; bp, 140-5°/ .0009 mm
R_1=R_2=C_6H_5 R_3=H.	84	mp, 96-98° (methanol) lit.[6], 94°	-	-	-
R_1=C_6H_5 R_2=CH_3; R_3=OCH_3	37	Colourless oil bp, 150°/.0075 mm; mp 97°	21	Colourless oil bp, 150°/ .0075 mm lit.[7], bp, 150°/ .0075 mm	-
R_1=C_6H_5; R_2=CH_3; R_3=H.	55	mp, 85° (methanol)	-	-	-
R_1=2-thienyl R_2=H; R_3=H.	2		61	Yellowish oil bp, 130°/ .08 mm	-
R_1=R_2=cyclohexyl * R_3= OCH_3	85	Colourless oil bp, 150°/ .5 mm	-	-	-

The reaction mixture was poured in cold water, basified, ether extracted and the product chromatographed over silica gel gr.II.

* This carbinol was cyclodehydrated by interaction with PPA at 98° for 30 minutes.

The formation of rearranged tetrahydroquinolines (IV) instead of the normal products (V) may be accounted for by postulating the intermediate formation of azetidines (VI) which then rearrange to give the observed products. The rearrangement of (VI) to (IV) will have to be accounted for by the assumption of a suprafacial sigmatropic rearrangement where there would be an inversion at C_2 atom in (VI)[2]. The rearrangements now reported are analogous to similar cases of rearrangement in carbocyclic series reported by Berson[3] and by Tisler[4].

In one case (III; $R_1 = C_6H_5$, $R_2 = H$, $R_3 = OCH_3$) the intermediate azetidine (VI; $R_1 = C_6H_5$, $R_2 = H$, $R_3 = OCH_3$) has also been isolated. This azetidine partially rearranged slowly to 7-methoxy-2-phenyl-1,2,3,4-tetrahydroquinoline on keeping at room temperature. The above azetidine and rearranged tetrahydroquinoline were distinguished from each other by their NMR (Fig.1) and mass spectra. In the azetidine the -NH proton was absent, whereas in the tetrahydroquinoline its presence was shown by D_2O exchange. The fact that in the rearranged 2,3-disubstituted tetrahydroquinolines (IV; $R_1 = R_2 = \phi$, $R_3 = H$, and $R_1 = \phi$, $R_2 = CH_3$, $R_3 = OCH_3$) the substituents are trans-located lends support to the intermediate formation of azetidines with the stereochemistry as shown in (VI).

The above experiments are summarised in Table 1. The structural assignments for the compounds reported are fully supported by their elemental analysis, IR, NMR and mass spectral data as well as their comparison with the authentic samples prepared by other routes. Details of the work will be reported shortly in Tetrahedron.

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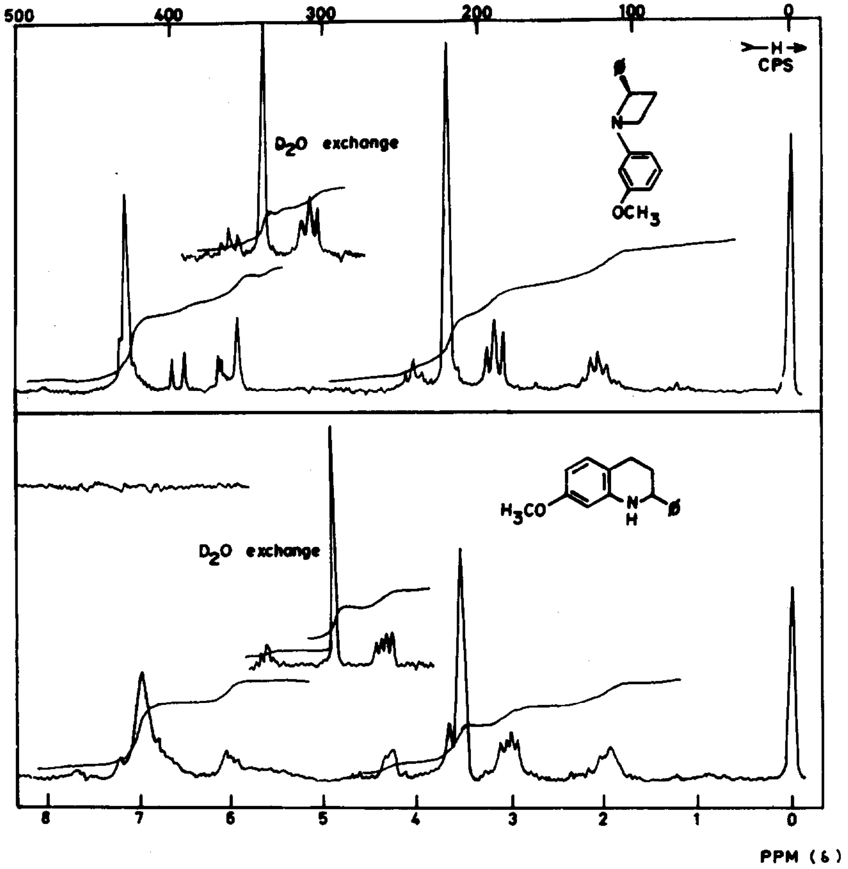

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