Tetrahedron Letters No. 21, pp 1867 - 1870, 1973. Pergamon Press. Printed in Great Britain.

A CONVENIENT SYNTHESIS OF N-ARYLAZETIDINES*

V.N. Gogte, S.B. Kulkarni and B.D. Tilak+

National Chemical Laboratory, Poona-8, India

(Received in UK 2 April 1973; accepted for publication 10 April 1973)

N-Arylazetidines have been proposed as reactive intermediates in the acid catalysed cyclodehydration of 1-arylamino-3-alkanols which give the rearranged 2-substituted-1,2,3,4-tetrahydroquinolines instead of the expected 4-substituted-1,2,3,4-tetrahydroquinolines[1]. We have reported the synthesis of 1-(3'-methoxyphenyl)-2-phenylazetidine by the treatment of 1-(3'-methoxyphenylamino)-3-phenylpropan-3-ol with 70 per cent sulphuric acid[1]. However, this method failed to give N-arylazetidines in many cases and only the rearranged tetrahydroquinolines were obtained as end products. In order to examine the problems in connection with the stereospecific ring opening of N-arylazetidines leading to the formation of tetrahydroquinolines, it was necessary to develop a better synthesis of N-arylazetidines carrying substituents in the azetidine ring. In the synthesis of azetidines by Deady et al[2] excepting the phenyl group attached to the nitrogen atom there were no substituents in the azetidine ring.

For the synthesis of N-arylazetidines from 1-arylamino-3-alkanols the reaction should be preferably carried out under basic conditions and involve the conversion of the γ-hydroxy group into a good leaving group. We have

---

* NCL Communication No.1692. This is Part VI of series 'Synthesis of Heterocyclic Compounds', Part V, Tetrahedron Letters, 4305 (1971)

+ To whom the enquiries should be addressed.

found that the conversion of the hydroxy group in carbinol (A) into oxophosphonium bromide group by treatment with triphenylphosphine dibromide in acetonitrile solution followed by interaction with triethylamine (2 moles) at -5° for 72 hr. leads to the formation of N-arylazetidines (B) along with the corresponding mixed tetrahydroquinolines (C and D) (Chart 1). Under these conditions some unreacted carbinol was recovered unchanged. Compounds A, B and mixed C and D were separated by column chromatography on silica gel. The results obtained are summarized in Table 1.

CHART 1

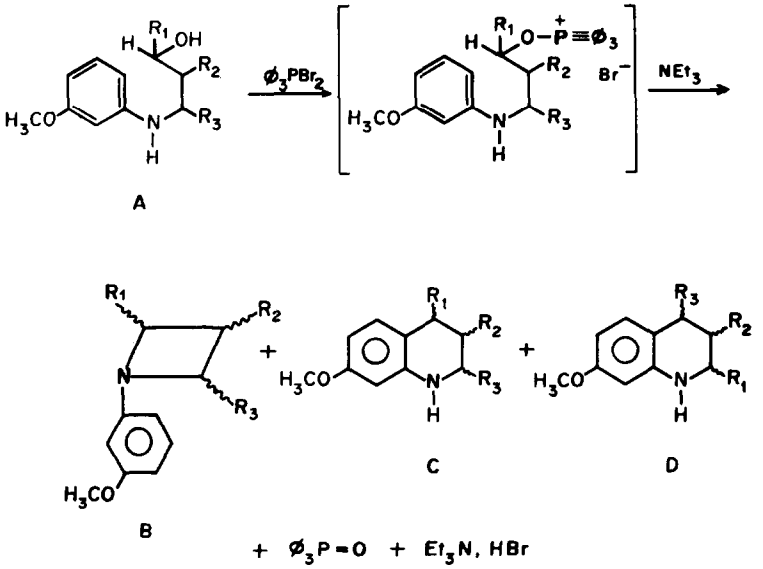

Table 1

No.	Carbinol A 5.0 g	Reaction Products			Azetidines (B) mp/bp (solvent)
		Unreacted Carbinol A g	Azetidine B g	Mixed Tetrahydroquinolines C and D; g	
I.	R_1=C_6H_5;R_2=R_3=H;	0.59	1.00	0.99	yellow oil; bp, 140-5°/ 9 x 10^{-4}mm
II.	R_1=C_6H_5;R_2=H; R_3=CH_3	0.45	0.46	1.21	colourless plates (methanol) mp, 89°
III.	R_1=CH_3;R_2=H; R_3=C_6H_5	1.03	2.32	0.58	-do-
IV.	R_1=C_6H_5;R_2=CH_3 R_3=H	0.51	0.43	1.41	colourless plates (methanol); mp, 94°
V.	R_1=CH_3;R_2=H; R_3=CH_3	0.42	0.84	0.55	yellow oil; bp, 100°/ 2.13 x 10^{-2} mm

It was observed that when R_1 and R_3 or R_1 and R_2 are phenyl substituents the reaction failed. In the case of (II), (III) and (IV) a mixture of two stereo-isomeric azetidines was obtained as revealed by two types of methyl doublets in their PMR spectra (Fig.1). These two stereoisomers could not be separated by conventional methods and attempts are under way to prepare them stereospecifically by pre-resolution of alkanols into erythro and threo components followed by cyclisation.

The azetidines were converted into the corresponding tetrahydroquinolines by pyrolysis at 290° and also by exposure to ultraviolet light from a medium pressure mercury vapour lamp.

The structural assignments of the compounds listed are fully

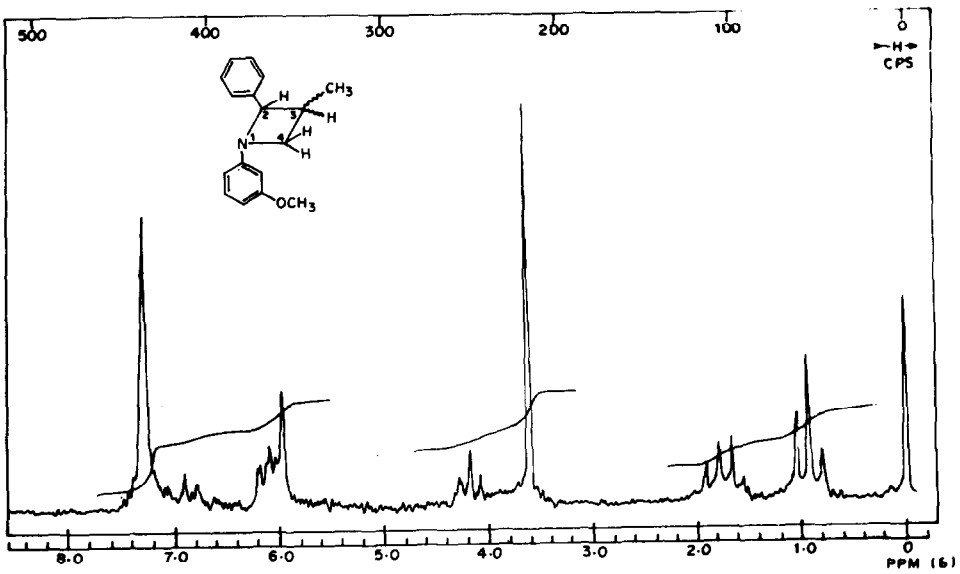

FIG. 1 PMR SPECTRUM OF 1-(3'METHOXYPHENYL)-3 METHYL-2-PHENYLAZETIDINE RECORDED IN CCl_4 AT 60 MHz

supported by their elemental analysis, IR, PMR and mass spectra.

Acknowledgement: The authors are thankful to the Council of Scientific and Industrial Research, New Delhi, for financial assistance.

REFERENCES

1. V.N.Gogte, H.M.El-Namaky, M.A.Salama and B.D.Tilak, Tetrahedron Letters, 3319 (1969)

2. L.W.Deady, R.D.Topsom, R.E.J.Hutchinson, J.Vaughan and G.J.Wright, Tetrahedron Letters, 1773 (1968)