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2-(3-Arylpropyl)pyridines were synthesized in 30-54% yields by the free-radical addition of toluene, o-, m-, and p-xylenes, and mesitylene to 2-vinylpyridine at 250-350°C. The products of rearrangement of the intermediate adduct radical with 1,3-H migration were isolated and identified.

The free-radical pyridylethylation of arylalkanes has not been studied. Arylalkylpyridines have pharmacological, herbicidal, fungicidal, and other forms of activity [1-4]; they are also intermediates in the synthesis of medicinals [5, 6]. The usual methods for their synthesis are complex [7].

We propose a method for the preparation of arylalkylpyridines by the free-radical pyridylethylation of arylalkanes. We investigated the addition of toluene, o-, m-, and $p-xy^{-1}$ lenes, and mesitylene to 2-vinylpyridine (2-VP) under thermal-initiation conditions.

The effect of the reaction conditions (the reagent ratio and the temperature) on the compositions and yields of products was studied in the case of the reaction of toluene with 2-VP. The results are presented in Table 1. The principal reaction product is 2-(3-phenylpropyl)pyridine (I). In addition to I, we also isolated [by preparative gas-liquid chromatography (GLC)] and identified the following compounds: 2'-(3-phenylpropen-1-yl)pyridine(II — the product of disproportionation of the adduct radical (R_{add})); 1, 3-di(2-pyridyl)propane (IVa) and 1,2-di(2-pyridyl)ethane (IVb), which are formed along with styrene (III) as a result of rearrangement of the adduct radical with 1,3 migration of a hydrogen atom and subsequent β decomposition of the rearranged adduct radical (R'_{add}); diphenylpropane (VI), which is the result of addition of the benzyl radical to styrene; dibenzyl (V), which is the product of quadratic chain termination; 2-VP dimers, viz., the linear 1,4-di(2-pyridyl)butane dimer (VIIa) and the cyclic 1,3-di(2-pyridyl)cyclobutane dimer (VIIb).

The most probable pathways for the formation of I-VII are shown in the scheme below:

thermolysis
ArCH₃
$$\longrightarrow$$
 ArCH₂

FABLE	1.	Free-Radical	Pyridylethyl	lation of	Arylalkanes
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Hydrocar- bon	Hydrocar- bon:2-VP molar ratio	Temp. °C	Time, h	Conv. of 2- VP. %	Yield b used in 1 11	based on an 1 the react $1 \vee (a,b)$	nt.of 2 ion, %	-VP	Amt.of resin, g
Toluene Toluene """ """ """ ""-Xylene The same p-Xylene o-Xylene Mesitylene	100 : 1 100 : 1 75 : 1 100 : 1 100 : 1 100 : 1 200 : 1 100 : 1 100 : 1 100 : 1 100 : 1 100 : 1	250 300 350 350 350 350 350 350 350 350 3	$ \begin{array}{c} 4 \\ 4 \\ 2 \\ 4 \\ 6 \\ 2 \\ 4 \\ 2 \\ 2 \\ 2 \\ 2 \\ 2 \\ 2 \\ 2 \\ 2 \\ 2 \\ 2$	78 84 75 90 91 97 81 95 96,5 99 98 98	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c} 7 \ (1,8) \\ 18 \ (2,6) \\ 26 \ (2,9) \\ 15 \ (5,5) \\ 28 \ (3) \\ 26 \ (3,3) \\ 23 \ (5,2) \\ 16 \ (2,3) \\ 12 \ (4) \\ 15 \ (4,6) \\ 13 \ (2,3) \\ 6 \ (2) \end{array} $	Traces Traces 4 5,6 7 10 5 16 7 11 9 1	16 18 3 1 Traces Traces 5 1 Traces	$\begin{array}{c} 6,2\\ 6,7\\ 4\\ 5,1\\ 4,5\\ 3,8\\ 4,2\\ 4,1\\ 5,5\\ 5,4\\ 3,8\end{array}$

*The yields of IV and VII are presented from the calculation that 0.5 mole of IV and VII is formed from 1 mole of 2-VP.

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(1)

$$ArCH_2 + PyCH = CH_2 \longrightarrow ArCH_2CH_2CHPy \qquad R_{add}$$
(2)

 $R_{add} + ArCH_3 \longrightarrow ArCH_2CH_2CH_2Py + ArCH_2$ (3)

$$R_{add} \xrightarrow{-H} ArCH_2CH = CHPy \quad II \tag{4}$$

$$R_{add} \xrightarrow{1,3-H} ArCHCH_2CH_2Py \xrightarrow{\beta-cleavage} ArCH=CH_2+PyCH_2$$

$$2P_yCH_2 \longrightarrow P_yCH_2CH_2P_y \qquad IV_b \qquad (7)$$

$$III + Ar\dot{C}H_2 \longrightarrow ArCH_2CH_2\dot{C}HAr \longrightarrow ArCH_2CH_2CH_2Ar \quad VI$$
(8)

$$2ArCH_2 \longrightarrow ArCH_2CH_2Ar \qquad V \tag{9}$$

$$2PyCH=CH_{2} \longrightarrow PyCH_{2}CH_{2}CH_{2}CH_{2}Py \qquad VIIa$$

$$Py-CH=CH_{2} \qquad (10)$$

$$CH_{2}-CH=Py \qquad VIIb$$

 $Ar = C_6H_5$; o-, p-, m-CH₃C₆H₄; 3,5(CH₃)₂C₆H₃; Py = 2-pyridy1

To confirm the structures of the products of the rearrangement of IV we used known methods to synthesize 1,3-di(2-pyridyl)propane by the reaction of 2-picoline with 2-VP in the presence of sodium [8]

Na

$$PyCH_3 + PyCH == CH_2 \longrightarrow PyCH_2CH_2CH_2Py,$$

and 1,2-di-(2-pyridyl)ethane by the reaction of 2-picoline with lithium in bromobenzene [9]
 Li, Br_2
 $PyCH_3 \longrightarrow PyCH_2CH_2Py.$

The model compounds were found to be identical to IVa,b.

The data in Table 1 show that the reactions of toluene with 2-VP require the use of temperatures on the order of 300-500°C; at 250-300°C the yield of I is not higher than 5%. The reaction temperature is the most important factor that affects the yield of I. An increase in the toluene:2-VP ratio also promotes an increase in the yield of I.

The need for the use of high temperature and a large excess of the hydrocarbon is explained by the pecularities of the nature of the reagents, which hinder the steps involving chain growth (2) and chain propagation (3). The fact of the formation of side products (II-VI) constitutes evidence for this. It is interesting to note that products similar to II-VI were not detected in the related free-radical cyanoethylation of arylalkanes with acrylonitrile under similar conditions [10]. This difference is evidently associated with the difference in the electronic and steric properties of 2-VP and acrylonitrile, which are ultimately responsible for the greater stability of the adduct radical in pyridylethylation as compared with the adduct radical formed in cyanoethylation. As a consequence of the increase in the stability of the adduct radical, the rates of its disproportionation and rearrangement become appreciable [steps (4) and (5)]. All of the factors that accelerate chain propagation therefore decrease the probability of the occurrence of side processes and promote an increase in the yield of adduct I. The most important factor that determines the rate of step (3) is the H-donor capacity of the addend. In the investigated series of hydrocarbons it increases in the order toluene, xylene, mesitylene [11]. This factor evidently determines the contribution of reactions (3) and (5) to the overall process. In fact, in the pyridylethylation of toluene reactions (3) and (5), judging from the yields of I and IV, proceed at approximately the same rate; reaction (3) is preferable with the xylenes, while step (3) is the primary process with mesitylene.

The yields of adducts I increase on passing from toluene to the xylenes and mesitylene; this is evidently associated with an increase in the nucleophilicity of the radicals generated from these hydrocarbons.

Аг	bp, °C (mm)	Found, %			Empirical	Calc., %		
		с	н	N	formula	С	н	N
C_6H_5 o-CH ₃ C ₆ H ₄ m-CH ₃ C ₆ H ₄ p-CH ₃ C ₆ H ₄ 3,5-(CH ₃) ₂ C ₆ H ₃	$\begin{array}{c} 149 - 150 \ (6) \\ 135 - 136 \ (3) \\ 157 - 159 \ (7) \\ 163 - 164 \ (7) \\ 159 - 161 \ (5) \end{array}$	85,4 85,2 85,1 85,3 85,3	7,5 8,0 8,2 8,3 8,4	7,0 6,5 6,5 6,6 6,1	$\begin{array}{c} C_{14}H_{15}N\\ C_{15}H_{17}N\\ C_{15}H_{17}N\\ C_{15}H_{17}N\\ C_{16}H_{17}N\\ C_{16}H_{19}N \end{array}$	85,3 85,3 85,3 85,3 85,3 85,3	7,6 8,1 8,1 8,1 8,5	7,1 6,6 6,6 6,6 6,2

TABLE 2. Characteristics of the 1:1 Adducts (I)

EXPERIMENTAL

The mass spectra were recorded with an MKh-1303 spectrometer at an ionizing voltage of 40 V. The PMR spectra were recorded with a JNM-4H-100 spectrometer with hexamethyldisiloxane as the internal standard and CCl₄ as the solvent.

The arylalkanes were dried over KOH and distilled and stored over sodium. The 2-VP was obtained by reaction of 2-picoline with 27% formaldehyde solution in an autoclave by the method in [13].

The addition of the arylalkanes to 2-VP was carried out in a 3-liter autoclave. The coefficient of filling of the autoclave was 0.6-0.7. Depending on the reaction temperature and the coefficient of filling of the autoclave, the pressure was varied from 10 to 80 atm. After removal of the bulk of the hydrocarbon by distillation, the concentrated reaction mixture was analyzed by GLC with the aid of 4-benzylpyridine as the internal standard. Distillation of the concentrated reaction mixture in vacuo gave fractions over the 10-15°C temperature range, which were then separated by preparative GLC. Analysis by GLC was carried out with a Varian chromatograph with a flame-ionization detector. For quantitative analysis we used 10% FFAP on Chromosorb W as the liquid phase; the vaporizer temperature was 250°C, the detector temperature was 260°C, the column temperature was 170-245°C (1 deg/min), the helium, hydrogen, and air flow rates were 18, 18, and 180 ml/min, respectively, and the metal column had dimensions 150 by 0.3 cm.

For preparative separation we used a 600 by 0.95 cm column filled with 20% FFAP on Chromosorb W (45/60 mesh). The temperature conditions were similar to those used above.

<u>Pyridylethylation of Toluene.</u> A concentrated reaction mixture (38 g) was obtained from 1214 g (13.2 mole) of toluene and 13.9 g (0.132 mole) of 2-VP. Vacuum distillation gave fractions with the following boiling points: I) 135-150°C (5 mm) (11.6 g); 2) 150-160°C (5 mm) (1.5 g). The following compounds were isolated from fractions 1 and 2 by preparative GLC.

 $\frac{32'-(3-\text{Phenylpropyl})\text{pyridine (I).}}{\text{phenyl}, 7.3 (1\text{H}, \gamma-\text{pyridine}), 2.65 (2\text{H}, \text{PyCH}_2), 2.45 (ArCH_2), and 2.0 ppm (2\text{H}, CH_2CH_2CH_2).}$ Mass spectrum: M⁺ 197. The results of elementary analysis are given in Table 2.

<u>2'-(3-Phenylpropen-1-yl)pyridine (II)</u>. PMR spectrum: 8.4, 7.3, 7.0, 2.5 (2H, ArCH₂); 5.03 (1H, CH₂CH=); 5.5 ppm (PyCH=). Mass spectrum: M⁴ 195. Found: C 85.9; H 6.6; N 7.1%. C₁₄H₁₃N. Calculated: C 86.1; H 6.7; N 7.2%.

<u>IVa.</u> PMR spectrum: 8.4, 7.3, 7.0, 2.75 (4H, PyCH₂); 2.25 ppm (2H, CH₂CH₂CH₂). Mass spectrum: M⁺ 198.

IVb. PMR spectrum: 8.3, 7.3, 7.0, 2.5 ppm (4H, PyCH₂). Mass spectrum: M⁺ 184.

Compound V had mp 51°C [14].

VI. PMR spectrum: 7.0 (10H, aromatic protons), 2.55 (4H, $C_6H_5CH_2$), and 2.0 ppm (2H, $CH_2CH_2CH_2$). Mass spectrum: M⁺ 196.

VIIa. PMR spectrum: 8.3, 7.3, 7.0, 2.6 (4H, PyCH₂); 1.8 ppm (4H, middle CH₂ groups). Mass spectrum: M⁺ 212.

VIIb. PMR spectrum: 8.3, 7.3, 7.0, 2.65 (2H, CHPy); 1.8 ppm (4H, CH₂). Mass spectrum: M⁺ 210.

<u>Pyridylethylation of m-Xylene</u>. A concentrated reaction mixture (23 g) was obtained from 1063 g (10 moles) of m-xylene and 10.5 g (0.1 mole) of 2-VP. Vacuum distillation (8 mm) gave two fractions: The first fraction (10.2 g) had bp 155-170°C, while the second fraction (1 g) had bp 175-180°C.

<u>Pyridylethylation of Mesitylene.</u> A concentrated reaction mixture (25 g) was obtained from 1256 g (10.5 moles) of mesitylene and 10.5 g (0.1 mole) of 2-VP. Vacuum distillation (6 mm) gave two fractions: The first fraction (11.4 g) had bp 160-170°C, while the second fraction (3.3 g) had bp 175-190°C.

Compounds I-VII with Ar = o-, m-, and $p-CH_3C_6H_4$ and $3,5-(CH_3)_2C_6H_3$ were isolated preparatively from the pyridylethylation of the xylenes and mesitylene. The PMR and mass spectra of these compounds are similar in character to the corresponding spectra of I-VII with Ar = C_6H_5 . The characteristics of the principal reaction products are given in Table 2.

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SYNTHESIS AND THREE-DIMENSIONAL STRUCTURES OF

3-(α -AMINO- and α -HYDROXYBENZYL)QUINUCLIDINES

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3-Substituted quinuclidines that contain a hydroxy or amino group in the side chain were synthesized by reduction of 3-benzoyl- and 3-benzoylmethylquinuclidines and their oximes. It is shown that the reduction of the ketones takes place stereospecifically to give one diastereomeric alcohol in both cases, whereas mixtures of diastereomeric 3-(α -aminobenzyl)quinuclidines are formed in the hydrogenation of their oximes. The configurations of the substances obtained were established on the basis of data from the PMR spectra.

The high biological activity of arylalkanolamines and arylalkylideneamines, which include noradrenaline, ephedrine, propanolol, etc., is widely known.

In a number of cases the activity is also retained when fragments that correspond to these compounds are included in mono- and bicyclic systems. The previously described 3-hy-

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