REACTION OF HYDROXY DERIVATIVES OF PIPERIDINES AND PYRIDINES WITH ACETYLENE UNDER PRESSURE

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Methods for the synthesis of vinyl ethers of N-(β-hydroxyethyl)-piperidine, 3-hydroxy-N-methylpiperidine, 2-(β-hydroxyethyl)pyridine, and 2-(hydroxypyridine) based on the addition of the corresponding derivatives to acetylene have been developed. Their hydrogenation forms the corresponding ethyl ethers.

Unsaturated heterocyclic compounds of the piperidine and pyridine series are characterized by a high reactivity and are the starting compounds for the synthesis of more complex substances with medicinal, ion-exchange, and other properties of practical value [1,2].

The vinyl ethers of this class of compound have been studied extremely inadequately. In view of this, it appeared to be of interest to investigate the reaction of acetylene with the hydroxy derivatives of some piperidines and pyridines. The starting materials for vinylation that we selected were N-(β-hydroxyethyl)-piperidine (I), 3-hydroxy-N-methylpiperidine (II), 2-(β-hydroxyethyl)pyridine (III), and 2-hydroxypyridine (IV).

When the piperidine derivatives I and II were heated with acetylene at 205–220° C in the presence of 30% KOH for 1 hr, the corresponding vinyl ethers V and VI were formed smoothly (see table).

Addition of the hydroxypyridines III and IV to acetylene requires lower temperatures (150–180° C). However, we were unable to synthesize 2-(β-vinyloxyethyl)-pyridine (VII) in the presence of caustic potash. In this case, when III was heated in an alkaline medium it underwent dehydration with the formation of 2-vinylpyridine [3]. The vinyl ether VII was obtained by using cadmium acetate as catalyst at 160° C. The yield of VII on direct vinylation amounted to 56%, while when VII was obtained from ethyl vinyl ether and III [4] it did not exceed 32%.

2-Hydroxypyridine (IV) exists in two tautomeric forms, a lactam and a hydroxy form [5–7]. It is considered that in the reaction of IV with acetylene in the presence of alkali and water the reaction takes place with the transfer of the active center and only N-vinylpyridone (VIII) is formed [8]. The latter was obtained previously by the condensation of the sodium salt of 2-hydroxypyridine with 2-chloroethylamine [9].

Assuming that IV can add acetylene in both tautomeric forms with the formation of the N-vinylpyridone VIII and 2-vinyloxypyridine, we continued our investigation of the vinylation of IV under various temperature conditions and attempted to separate the reaction products by chromatography.

Chromatography of the vinylation products in a nonfixed layer of alumina in the absolute benzene system showed that they yielded two spots, neither of which was due to the initial IV. By means of liquid chromatography the reaction mixture was separated into several fractions and the N-vinylpyridone (VIII) was isolated in the individual state (R_f 0.074). Its IR spectrum contains an absorption band at 1680 cm^{-1} which is characteristic for the stretching vibrations of a carbonyl group and one at 1640 cm^{-1} which is due to the C=C vibrations of the terminal vinyl group.

The IR spectrum of the second substance (R_f 0.89) contained the same bands at 1680 and 1640 cm^{-1}, but with different intensities. New bands had appeared in the 2950–2850 cm^{-1} region. Because the amount of this substance was very small, it has not yet been possible to determine its properties and establish its structure. The vinylation of IV was carried out at a higher temperature than in previous work [8] and without the addition of water to the reaction mixture. At 180° C in the presence of 30% KOH, the yield of VIII increased to 68%.

All the vinyloxypiperidines and vinyloxypyridines obtained readily form picrates and undergo hydrogenation over Raney nickel to the corresponding ethoxy derivatives, the properties of which are given in the table. Under the influence of dil H_2SO_4, compounds V–VIII are hydrolyzed with the formation of acetaldehyde.

The structure of the vinyloxy derivatives V–VII is also confirmed by their spectroscopic characteristics. Their IR spectra contain bands in the 1638–1640 and 1200–1202 cm^{-1} regions due to the presence of $-CH=CH_2$ and ethereal C—O—C groups.

EXPERIMENTAL

N-(β-Vinyloxyethyl)piperidine (V). A 1-liter autoclave was charged with 20 g (0.15 mole) of the piperidine I [bp 199° C (735 mm); n_D^{20} 1.4780], 6.6 g of KOH, and 120 ml of dioxane, and acetylene was passed in from a cylinder under a pressure of 15 atm. The reaction mixture was heated at 205–215° C for 1 hr. After the elimination of the solvent, the reaction products were washed several times with 5% KOH solution and then with water and were dried with potassium carbonate. Vacuum distillation in a current of nitrogen yielded 15 g of the ether V.

N-Methyl-3-vinyloxypiperidine (VI). The vinylation of 10 g (0.09 mole) of the piperidine II [bp 179–180° C (727 mm); n_D^{20} 1.4740] in the presence of 3.3 g of KOH in 50 ml of dioxane at 200° C for 40 min yielded 10.3 g of compound VI.

Properties of the Vinyl and Ethyl Ethers of Hydroxypiperidines and Hydroxypyridines

Compound	Name	Bp, °C (pressure, mm)	n_D^{20}	d_4^{20}	MR_D		Empirical formula	Found, %			Calculated, %			Picrate				Yield, %
					found	calculated		C	H	N	C	H	N	mp, °C	empirical formula	N, %		
																found	calculated	
V	N-(β-Vinyloxyethyl)piperidine	68—69 (7)	1.4676	0.9166	47.00	46.68	$C_9H_{17}NO$	59.70	11.06	9.21	69.63	11.04	9.02	78—79	$C_9H_{17}NO \cdot C_6H_3N_3O_7$	14.88; 14.58	14.58	63
VI	3-Vinyloxy-N-methylpiperidine	52—53 (10)	1.4620	0.9202	42.19	42.06	$C_8H_{15}NO$	68.42	10.67	9.66	68.04	10.77	9.92	125	$C_8H_{15}NO \cdot C_6H_3N_3O_7$	15.31; 15.22	15.14	82
VII	2-(β-Vinyloxyethyl)pyridine	94—95 (10)	1.5118	1.0114	44.24	44.48	$C_9H_{11}NO$	72.39	7.55	9.68	72.45	7.43	9.39	104—105	$C_9H_{11}NO \cdot C_6H_3N_3O_7$	15.01; 15.18	14.81	56
VIII	N-Vinylpyridone	88 (2,5)	1.5892	1.1223	36.36	34.88	C_7H_7NO	69.30	5.80	11.77	69.40	5.82	11.56	91—92	$C_7H_7NO \cdot C_6H_3N_3O_7$	15.90; 16.08	15.99	68
IX	N-(β-Ethoxyethyl)piperidine	49 (4)	1.4500	0.8872	47.61	47.15	$C_9H_{19}NO$	68.90	12.00	8.53	68.74	12.18	8.90	73—74	$C_9H_{19}NO \cdot C_6H_3N_3O_7$	14.18	14.50	85
X	3-Ethoxy-N-methylpiperidine	62 (16)	1.4555	0.9078	42.81	42.53	$C_8H_{17}NO$	67.40	11.93	—	67.07	11.96	9.79	118—119	$C_8H_{17}NO \cdot C_6H_3N_3O_7$	15.29	15.05	61
XI	2-(β-Ethoxyethyl)pyridine	90—91 (10)	1.4845	0.9611	45.04	44.85	$C_9H_{13}NO$	71.24	8.68	9.39	71.49	8.66	9.26	102—103	$C_9H_{13}NO \cdot C_6H_3N_3O_7$	14.70	14.73	87

Vinyl ether of 2-(β-hydroxyethyl)pyridine (VII). A mixture of 20.3 g of the pyridine III [bp 114–116° C (9 mm) n_D^{20} 1.5380; d_4^{20} 1.2983], 4.35 g of $(CH_3COO)_2Cd \cdot 2H_2O$, and 50 ml of benzene was heated in an atmosphere of acetylene at 150–155° C for 45 min. The reaction products were worked up in a similar manner to the case of compound V. The yield of VII was 13.3 g.

N-Vinylpyridone (VIII). The vinylation of 2-hydroxypyridine was carried out at 180–190° C for 30 min with 30% KOH. The yield of VIII was 68%.

The hydrolysis of compounds V–VIII (0.10–0.15 g) was carried out with 20 ml of 2% H_2SO_4 at 96–98° C for 6 hr. The yields of acetaldehyde ranged from 33% (VIII) to 84% (VII).

N-(β-Ethoxyethyl)piperidine (IX). A mixture of 1.2 g of the ether V, 5 ml of anhydrous ethanol, and 0.8 g of Raney nickel was placed in a glass hydrogenation device. Hydrogen was fed in until absorption ceased. Then the catalyst was filtered off, the solvent was evaporated off, and the residue was distilled in vacuum. The hydrogenation of compounds VI and VII was carried out similarly. The properties of compounds IX–XI obtained and their picrates are given in the table. In the IR spectra of IX–XI the band at 1640 cm^{-1} had disappeared.

The IR spectra were measured in the 700–3500 cm^{-1} region on a UR-10 infrared spectrometer. The samples of all the liquid substances were prepared in the form of microlayers.

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