

# AMINOMETHYLATION OF THE $\beta$ - AND $\gamma$ -ISOMERS OF 1-ALLYL-3-METHYL-4-ETHYNYL-4-PIPERIDINOL

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Condensation of the  $\beta$ - and  $\gamma$ -isomers of 1-allyl-3-methyl-4-ethynyl-4-piperidinol with dimethyl- and diethylamine in benzene or dioxane and paraformaldehyde in the presence of a catalytic amount of cuprous chloride has given the  $\beta$ - and  $\gamma$ -isomers of 1-allyl-3-methyl-4-(3'-dialkylamino-1'-propynyl)-4-piperidinol.

The Mannich aminomethylation of heterocyclic acetylenic alcohols has not been investigated very extensively.

We were interested in the  $\beta$ - and  $\gamma$ -isomers of 1-allyl-3-methyl-4-(3'-dialkylamino-1'-propynyl)-4-piperidinols (III-VI), which we have obtained by condensation of the geometrical  $\beta$ - and  $\gamma$ -isomers of 1-allyl-3-methyl-4-ethynyl-4-piperidinol (I and II) with paraformaldehyde and secondary amines in the presence of catalytic amounts of cuprous chloride in dioxane or benzene solution, according to the following scheme.

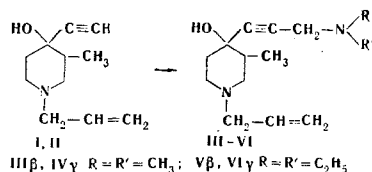
TABLE 1. Properties of  $\beta$ - and  $\gamma$ -1-Allyl-3-methyl-4-(3'-dialkylamino-1'-propynyl)-4-piperidinols and Their Dihydrochlorides\*

Compound	bp, °C (mm)	$d_4^{20}$	$n_D^{20}$	$M_{RD}$		Molecular formula	Found, %			Calculated, %			$R_f$	Yield, %
				Found	Calculated		C	H	N	C	H	N		
III $\beta$	110—111 (4)	0.992	1.4975	71.85	71.93	$C_{14}H_{24}N_2O$	71.58	10.07	11.60	71.14	10.23	11.85	0.24	66.4
IV $\gamma$	113—114 (4)	0.982	1.4983	71.78	71.94		70.87	9.92	11.60				0.76	68.0
V $\beta$	114—115 (5)	0.910	1.5005	82.57	82.69	$C_{16}H_{28}N_2O$	72.75	10.90	10.94	72.68	10.67	10.59	0.23	64.5
VI $\gamma$	97—98 (5)	0.910	1.4980	82.58	82.70		72.27	10.71	10.72				0.78	63.4

\* III $\beta$ ·2HCl. mp 186–187°C. Found, %: C 54.17; H 8.45; N 9.12; Cl 22.65. Calculated for  $C_{14}H_{24}N_2O \cdot 2HCl$ , %: C 54.50; H 8.42; N 9.07; Cl 23.16. IV $\gamma$ ·2HCl. mp 185–186°C. Found, %: C 54.24; H 8.40; N 9.11; Cl 22.70. V $\beta$ ·2HCl. mp 221–222°C (decomp.). Found, %: C 57.18; H 9.03; N 8.22; Cl 21.10. Calculated for  $C_{16}H_{28}N_2O \cdot 2HCl$ , %: C 57.20; H 8.70; N 8.20. VI $\gamma$ ·2HCl. mp 197–198°C. Found, %: C 57.18; H 8.65; N 8.17; Cl 21.38.

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The new amino alcohols III-VI were viscous, yellow liquids. Their physicochemical constants are given in Table 1.

## EXPERIMENTAL

A mixture of 1.8 g (0.01 mole) of piperidinols (I and II), 0.01 mole of 33% aqueous solution of the secondary amine, 0.45 g (0.015 mole) of paraformaldehyde, and a catalytic amount of cuprous chloride in 25 ml of anhydrous dioxane or benzene was heated on a boiling water bath with stirring for 5-14 hr. The mixture was cooled, treated with aqueous sodium carbonate, and extracted with ether. The ether extract was dried over potassium carbonate, the ether removed, and the residue was fractionated in vacuo.

Dihydrochlorides of aminopropynyl alcohols III-VI (see table 1) were obtained by addition of ethereal HCl to an ether solution of the base, followed by two recrystallizations from an acetone-ethanol mixture.

The purity of these aminopropynyl alcohols was checked by thin layer chromatography on alumina (grade II activity) in ether-acetone-methanol (7:3:1) and benzene-acetone (1:1) mixtures. The  $R_f$  values are given in the table.

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