ACETYLENIC AMINES, DERIVATIVES OF

p-MORPHOLINO- AND p-BROMOPHENYLACETYLENES

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Diacetylenic amines, derivatives of p-diethynylbenzene with the general formula



have a high physiological activity, and some of them are recommended as medical drugs [1, 2].

To study the relationship between the structure of aromatic acetylenic amines and their biological activity in more detail, we synthesized a series of acetylenic and diacetylenic amines from p-morpholino-phenylacetylene (I) and p-bromophenylacetylene (II) by Mannich and Chodkiewicz — Cadiot reactions. Thus, the following amines were prepared



Under normal conditions $(90-95^{\circ})$, the Mannich reaction with (II) proceeds quite readily. The dihydrochlorides of bases (III)-(V) and the hydrochlorides of bases (VI-VIII) were obtained by adding a saturated solution of HCl in absolute ether to ether solutions of the bases. The structure of all the compounds obtained was confirmed by elementary analysis.

EXPERIMENTAL METHOD

The synthesis of p-morpholinophenylacetylene has been described in [3]. 1-Bromo-3-morpholino-1-propyne and 1-bromo-3-piperidino-1-propyne were prepared by the method given in [4].

1-(p-Morpholinophenyl)-3-morpholino-1-propyne (V). A solution of 1 g of (I) in 10 ml of dioxane was added at 95° in a nitrogen current to a mixture of 0.18 g of CH₂O, 0.5 g of morpholine, 0.01 g of CuCl in 20 ml of dioxane. The reaction was followed by means of GLC (a "Vybukhokhrom" chromatograph, a column (2 m) with 5% XE-60 on chromatone, gas carrier N₂) from the disappearance of (I). The reaction

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Compound	Amines	Yield, 7/0	mp. °C	Empirical formula	Found Calc.			lo l	Dihydrochloride	
					c	н	Br	N	mp, °C	found Cl. %
(III)	1-(p-Morpholino- phenyl)-3-diethyl- amino-1-propyne 1-(p-Morpholino-	85	43	C17H24N2O	75,08	8,86 8,88	-	10,10 10,30	200202	
(IV)	phenyl)-3-piperidino -1-propyne	82	79,5-81	C ₁₈ H ₂₄ N ₂ O	75,83	$\frac{8,47}{8,51}$	_	$\frac{9,65}{9,72}$	210	19,94 19,85
(VII)	1-(p-Bromophenyl)- 3-piperidino-1- propyne 1-(p-Morpholino- phenyl)-S-piperi-	8 9	bp 143- 144 (5 mm)	C13Hi6NBr	58,70 58,65	<u>6,16</u> 6,06	29,98 30,02		170171	$\frac{\underline{11,32}}{\underline{11,72}}$
(VIII)	dino-1,3-penta- diyne	82	37-38	C ₁₄ H ₁₆ NBr	60,41 60,44	5,93 5,80	28,09	-	225—226	$\tfrac{\underline{11,06}}{\underline{11,27}}$
(XI)	3-diethylamino- 1-propyne	90	85	C20H24N2O	-		-	$\frac{9,04}{9,09}$	—	

TABLE 1. Acetylenic and Diacetylenic Amines, Derivatives of p-Morpholino- and p-Bromophenylacetylene

was essentially concluded after 60 min. The reaction mixture was diluted with water and extracted by ether. The ether extract was dried over K_2CO_3 and passed through a thin layer of Al_2O_3 (Grade II). The yield of (V) was 1.46 g (98%), mp 90-91° (from heptane). Found: C 71.12, H 7.80, N 9.67%. $C_{17}H_{22}N_2O_2$. Calculated: C 71.29, H 7.81, N 9.78%. Dihydrochloride of (V), mp 220° (dec). Found: Cl 19.78%. $C_{17}H_{22}N_2O_2 \cdot 2HCl$. Calculated: C 19.74%.

The condensation of (I) with diethylamine and piperidine was carried out similarly. The yield, the constants, and the data of the elementary analysis of the products are given in Table 1.

<u>1-(p-Bromophenyl)-3-morpholino-1-propyne (VIII).</u> A solution of 1.0 g of (II) in 10 ml of dioxane was added at 95° in a N₂ current to a mixture of 0.17 g of CH₂O, 0.48 g of morpholine and 0.01 g of CuCl in 20 ml of dioxane. The course of the reaction was followed by GLC from the disappearance of (II). The duration of the reaction was 30 min. The mixture was processed as described above. The yield of (VIII) was 1.35 g (88%), mp 52.5-53.5° (from heptane). Found: C 55.81, H 5.11, Br 28.52%. C₁₃H₁₄BrNO. Calculated: C 55.73, H 5.04, Br 28.52%. Hydrochloride, mp 230-231°. Found: Cl 11.06%. C₁₃H₁₅NOBrCl. Calculated: Cl 11.20%.

Compounds (VI) and (VII) were obtained similarly.

<u>1-(p-Morpholinophenyl)-5-morpholino-1,3-pentadiyne (XII).</u> A 7-ml portion of a 40% solution of $C_{2}H_{5}NH_{2}$ in $CH_{3}OH$ was added to a mixture of 2 g of (1), 0.01 g of CuCl, and 0.1 g of $NH_{2}OH \cdot HCl$ in 15 ml of $CH_{3}OH$. Then, with a vigorous stirring, 2 g of (X) were added dropwise in a N_{2} current. As the oxidation of CuCl progressed, the mixture turned green. To deoxidize it, $NH_{2}OH \cdot HCl$ was added. One hour after the addition of (X), the temperature of the reaction mixture was adjusted to 35°, and the mixture was held at this temperature for 3 hours, and then diluted with water and extracted by ether. The yield of (XII) was 94%, mp 90° (from methanol). Found: N 8.82%. $C_{19}H_{22}N_{2}O_{2}$. Calculated: N 9.03%.

Compound (I) reacted with (IX) to yield compound (XI) (see Table 1).

CONCLUSIONS

A series of amino derivatives of p-morpholino- and p-bromophenylacetylene was prepared.

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