SYNTHESIS OF 4-ARYLMORPHOLINE-2,3-DIONES BY THE REACTION OF N-(2-HYDROXYETHYL)ARYLAMINES WITH DIETHYL OXALATE

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The corresponding 4-arylmorpholine-2,3-diones were obtained by the reaction of N-(2-hydroxyethyl)aniline, N-(2-hydroxypropyl)aniline, N-(2-hydroxyethyl)-p-chloroaniline, and N-(2-hydroxyethyl)-p-anisidine with diethyl oxalate. The N-(2-hydroxyethyl)-o-, p-, and m-toluidines and N-(2-hydroxyethyl)-o-anisidine form 1,4-(ditolyl)piperazines and 1,4-di-(o-anisyl)piperazine,

4-Phenylmorpholine-2,3-dione was previously obtained from N-(2-hydroxyethyl)aniline and diethyl oxalate [1]. We have studied the reactions of N-(2-hydroxyethyl)aniline (I), N-(2-hydroxypropyl)aniline (II), N-(2-hydroxyethyl)-p-chloroaniline (III), N-(2-hydroxyethyl)-o-anisidine (IV), N-(2-hydroxyethyl)-p-anisidine (V), N-3-methoxy-2-hydroxypropylaniline (VI), and the isomeric N-(2-hydroxyethyl)toluidines (VII-IX) with diethyl oxalate. The formation of 4-arylmorpholine - 2,3-diones (1) or the corresponding oxamides (2) is possible in this process.

I, II, III, and V react with diethyl oxalate via route (1).

A detailed study of the reaction of I with diethyl oxalate indicated that the optimum conditions for obtaining 4-phenylmorpholine-2,3-dione (X) involve heating equimolecular amounts of the reagents for several hours at 130-140°C without a solvent. Compound X is obtained in 27% yield by refluxing equimolecular amounts of amino alcohol I and diethyl oxalate for 5 h in toluene; X is not formed under the same conditions in ethanol.



The structures of the 4-arylmorpholine-2,3-diones (X-XIII) are confirmed by the IR spectra, in which absorption bands characteristic for the N-C < 0 group (1685-1690 cm⁻¹) in the ring and bands at 1740-1750 cm⁻¹, which correspond to vibration of the -C < 0 group in the saturated ring, are absent.

4-Phenyl-6-methoxymethylmorpholine-2,3-dione could not be obtained from III [2] and diethyl oxalate.

The products of the reaction of V and VII-IX with diethyl oxalate were the corresponding 1,4-ditolylpiperazines (XIV-XVI) and 1,4-di(o-anisyl)piperazine (XVII) [3]. It may be supposed that the corresponding

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	Yield, η_{b}		55,5	26,9	46,4	Quanti- tative	11,3	24,7	25,5	22,3
FOUNCES OF THE REACTION OF N-12-TIJULOXYAIRY1/ALYIATHINGS WINT DIGUNT OVALATE	Calculated, 7/0	N	7,33	6,82	6,15	6,27	10,52			9,01
		н	4,71	5,4	3,8	5,01	8,26			11,05
		υ	62,82	64,4	53,2	59,8	81,2			69,6
	-	z	7,55 7,53	6,81 7,05	6,03 6,02	6,27 6,21	10,14 10,16	10,28 10,34	10,59 10,54	8,68 8,74
	Found, %	Н	4,86 4,89	5,1 5,2	3,64 3,68	4,93 4,87	8,05 8,18	8,14 8,13	8,7 8,67	10,96 10,83
		υ	63,28 63,44	64,24 63,96	53,12 52,98	59,75 59,63	81,70 81,60	81,52 81,48	81,04 81,02	69,45 69,24
	Empirical formula		C ₁₀ H ₉ NO ₃	C ₁₁ H ₁₂ NO ₃	C ₁₀ H ₈ CINO ₃	C ₁₁ H ₁₁ NO4	C ₁₈ H ₂₂ N ₂	$C_{18}H_{22}N_{2}$	C ₁₈ H ₂₂ N ₂	C ₁₈ H ₂₂ N ₂ O ₂
	mp (crystalliza- tion solvent)		162-163 (Alcohol)	154-155 (Benzene)	163-164 (Alcohol)	129—130 (Alcohol)	172173 (Metha- nol)	125126 (Metha- noi)	185	171—172 (Chloro- form - petroleum ether (1:2)
	Reac- tion time, h		ۍ م	ø	9	-	ŝ	8	ø	0
	Reaction temp., °C		130—140	135145	140—150	130—140	135—140	140145	140145	145—150
	R		Н	CH ₃	Н	Н	Н	Н	Н	Ξ
- - -	×		Н	Н	p-Cl	p-CH ₃ O	o-CH ₃	m-CH ₃	p-CH ₃	o-CH ₃ O
TAD	Com-	pumod	×	ΙХ	ШХ	ШХ	XIV	XV	IVX	ПУХ

TABLE 1. Products of the Reaction of N-(2-Hydroxyalkyl)arylamines with Diethyl Oxalate

4-tolylmorpholine-2,3-diones and 4-(o-anisyl)morpholine-2,3-dione are formed initially and then decompose with CO and CO_2 evolution under the experimental conditions.*

$$2RC_{6}H_{4}NHCH_{2}CH_{2}OH + 2(COOC_{2}H_{5})_{2} \rightarrow 2\left[\begin{array}{c}O & O \\ \parallel & \parallel \\ RC_{6}H_{4}N \\ \end{array}\right] \rightarrow RC_{6}H_{4}N \\ NC_{6}H_{4}R + 2CO + 2CO_{2} \\ XIV - XVII \end{array}\right]$$

The IR spectra of XIV-XVII do not contain absorption bands characteristic for N-C and

 $-C \langle 0 \\ 0 - 0 \rangle$ groups in the ring.

The synthesized compounds are of interest as possible physiologically active substances.

EXPERIMENTAL

<u>Reaction of N-(2-Hydroxyalkyl)arylamines with Diethyl Oxalate</u>. Equimolecular amounts of the N-(2-hydroxyethyl)arylamine and diethyl oxalate were placed in a two-necked flask equipped with a condenser set for distillation and a thermometer. The mixture was heated until ethanol formation ceased. The reaction mass began to solidify on standing; after recrystallization the products were white crystals (Table 1).

LITERATURE CITED

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The formation of CO_2 was confirmed by reaction with $Ba(OH)_2$.