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BEHAVIOR OF ALLYLATES AND PROPARGYLATES OF p- AND m-BIS(3-DIALKYLAMINO-1-PROPYNYL)BENZENES IN AQUEOUS ALKALINE MEDIUM*

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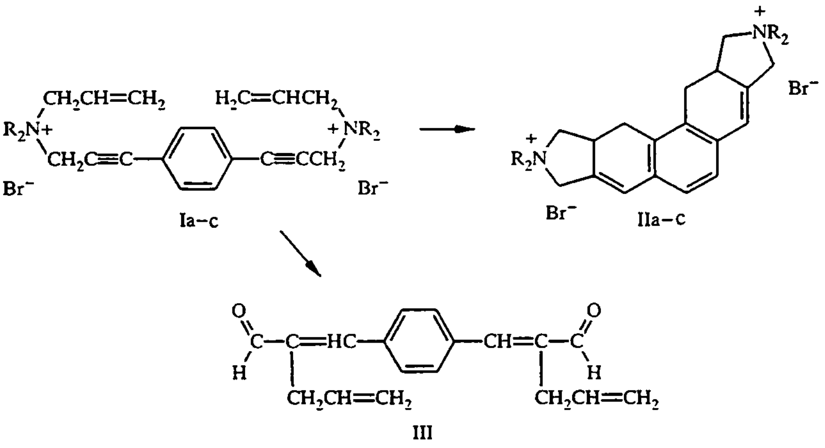
p-Bis[3-dialkyl-(2-propenyl)ammonio-1-propynyl]benzene dibromide is subject to two-stage cyclization and rearrangement—decomposition under base catalysis conditions. The possibility of a two-stage cyclization of m-bis[3-dialkyl-(2-propynyl)-ammonio-1-propynyl]benzene dibromide with the formation of benzo[5,6:5'6'-a,c]di-(2,2-dialkylisoindolinium) dibromide in quantitative yield has been shown.

It has been established that p-bis[3-dialkyl-(2-propynyl)ammonio-1-propynyl]benzene dibromides under base catalysis conditions undergo a two-stage cyclization with evolution of heat with the formation of benzo[5,6:5',6'-*a*,c]di-(2,2-dialkylisoindolinium) dibromides [2]. While continuing investigations in this area we studied the behavior of p-bis[3-dialkyl-(2-propenyl)ammonio-1-propynyl]benzene dibromides (Ia-c) towards aqueous alkali. Salts (Ia-c) underwent two-stage cyclization with the formation of benzo[5,6:5',6'-*a*,c]di-(2,2-dialkyl-3*a*,4-dihydroisoindolinium) dibromides (IIa-c) in yields of 35, 42, and 39% respectively and rearrangement—decomposition (12-18%) on stepwise addition of alkali at a molar ratio of salt—base of 1:0.8 and heating (90°C, 6 h).


Ia–c

IIa–c

III

I, II a $R_2 = Me_2$, b $R_2 = Et_2$, c $R_2 = (CH_2)_2O(CH_2)_2$

Dark colored salts (30-35%) were also isolated in addition to compounds (IIa-c). These dissolved readily in alcohol and solidified rapidly in the air.

The behavior of m-bis[3-dialkyl-(2-propynyl)ammonio-1-propynyl]benzene dibromides (IVa-d) under conditions of base catalysis was studied to ascertain the possibility of two-stage cyclization. We then considered developing a more convenient route of synthesis of potentially biologically active benzo[5,6:5',6'-*a*,c]di-(2,2-dialkylisoindolinium) dibromides [2].

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TABLE 1. Characteristics of the Initial (Ia-c) and Cyclic (IIa-c) Ammonium Salts

Compound	Empirical formula	mp, °C (from abs. ethanol)	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)
Ia	$C_{22}H_{30}Br_2N_2$	195	930, 950, 990, 1510, 1545, 1570, 2240, 3010, 3040, 3090	269 (4,86), 288 (4,84)
Ib	$C_{28}H_{38}Br_2N_2$	207	850, 900, 930, 950, 960, 990, 1500, 1640, 2240, 3050, 3090	268 (4,77), 272 (4,75)
Ic	$C_{26}H_{34}Br_2N_2O_2$	173	840, 910, 930, 990, 1490, 1510, 1640, 2220, 3090	210 (4,67), 265 (4,95), 280 (4,93)

Compound	mp, °C (from water)	R_f	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	Yield, %
IIa†	257	0,42	810, 1600, 1630	235 (4,89), 244 (4,87), 318 (4,65), 327 (4,54)	35
IIb	280	0,53	815, 1590, 1635	230 (4,45), 238 (4,64), 245 (4,62), 320 (4,38), 333 (4,23)	42
IIc	340	0,44	810, 1600, 1630	235 (4,89), 245 (4,62), 320 (4,38), 327 (4,54)	39

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*TLC was carried out on Silufol UV 254 plates in n-butanol–ethanol–water–acetic acid, 8:2:3:1.

†Compounds (Ia-c) and (IIa-c) are isomers.

TABLE 2. Characteristics of the Initial (IVa-d) and Cyclic (Va-d) Salts

Compound	Empirical formula	mp, °C	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	Compound †	mp, °C
IVa	$C_{22}H_{26}Br_2N_2$	*	750, 1500, 1520, 2130, 2240, 3160	234 (4,68), 267 (4,08), 279 (4,00)	Va	260-261
IVb	$C_{26}H_{30}Br_2N_2$	*	750, 1500, 1520, 2130, 2240, 3160	206 (4,72), 215 (4,64), 267 (4,96), 280 (4,93)	Vb	242‡
IVc	$C_{28}H_{34}Br_2N_2$	140	700, 740, 1590, 1660, 2130, 2250	234 (4,68), 267 (4,08), 279 (4,00)	Vc	270
IVd	$C_{26}H_{30}Br_2N_2O_2$	135	700, 740, 1560, 1590, 2130, 2250	234 (4,68), 267 (4,08), 279 (4,00)	Vd	327

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*Hygroscopic.

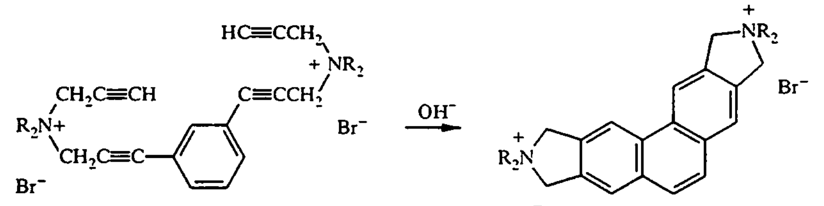
†Compounds (IVa-d) and (Va-d) are isomers.

‡The cyclization products (Va-d) gave no depression of melting point with authentic samples from [2]. The mp of salt (Vb) in the literature [2] was erroneously given as 272°C in place of 242°C.

Like the bis para derivatives, salts (IVa-d) were cyclized in the presence of a catalytic amount of aqueous alkali with evolution of heat forming salts (Va-d) almost quantitatively. These gave no depression of melting point with authentic samples from [2] (Table 2).

TABLE 3. Characteristics of m-Bis(3-dialkylamino-1-propynyl)benzenes (VI)-(IX)

Compound	R_2	Empirical formula	bp, °C (mm Hg)	IR spectrum, ν, cm^{-1}	mp picrate, °C	Yield, %
VI	$(CH_3)_2$	$C_{16}H_{20}N_2$	138 (3)	690, 800, 1500, 1560, 1580, 3020, 3060	156	63
VII	$(CH_2)_4$	$C_{20}H_{24}N_2$	212 (3)	700, 1565, 1590, 2240, 3060	149	60
VIII	$(CH_2)_5$	$C_{22}H_{28}N_2$	220 (3)	700, 770, 1500, 1575, 1590, 2240, 3030, 3060, 3070	205	65
IX	$(CH_2)_2O(CH_2)_2$	$C_{20}H_{24}N_2O_2$	230 (3)	710, 785, 1500, 1570, 1585, 2240, 3030, 3050, 3070	166	63



IVa-d Va-d

IV, V a $R_2 = Me_2$, b $R_2 = (CH_2)_4$, c $R_2 = (CH_2)_5$, d $R_2 = (CH_2)_2O(CH_2)_2$

The raw material for obtaining the initial m-bis(3-dialkylamino-1-propynyl)benzenes (VI)-(IX) is technical divinylbenzene which is a mixture of p- and m-divinyl-benzenes (45-55%), p- and m-ethylethynylbenzenes (40-45%), and m-ethylbenzene (<5%). The content of p-divinylbenzene in the mixture is 18%. Following bromination of the mixture p-divinylbenzene tetrabromide, being poorly soluble in chloroform, was separated from the other bromides by filtration. Dehydrobromination of the mixture of bromides soluble in chloroform gave a mixture consisting of m-diethynyl-, and p- and m-ethylethynylbenzenes. Isolation of them in a pure state from this mixture was not possible. A mixture of mono- and diamines must be formed from this mixture by the Mannich reaction. For participation in the Mannich reaction the duration of heating (at 90°C) is 4-5 h for p-divinylbenzene [3] and 50-55 h for arylacetylenes. However we established that heating the above mixture at 90°C with the appropriate secondary amine and paraformaldehyde for 12-15 h gave chromatographically pure bis(3-dialkylamino-1-propynyl)benzenes (VI)-(IX). The yields in the pure state after a second distillation were 60-65% (Table 3). Under these conditions a mixture of dialkyl-m(and p)-ethylphenylpropargylamines is also formed in 35-40% overall yield. The yields of diamines and monoamines are calculated on the initial acetylenes present in the mixture.

Absorption bands characteristic of the initial salts (Ia-c) for a doubly substituted C≡C bond at 2240, a p-substituted benzene ring at 850, and a monosubstituted C=C bond at 910, 960, 1640, and 3090 cm^{-1} were absent from the IR spectra of the cyclic salts (IIa-c). Absorption bands characteristic of a 1,2,3,4-substituted benzene ring and a conjugated diene system at 810 and 1600, 1630 cm^{-1} respectively were detected for salts (IIa-c).

In the UV spectra of the initial salts (Ia-c) the conjugation of the benzene ring with the acetylenic bond leads to a displacement of the absorption band of the benzene ring to the longer wave region (268, 270 nm). As a result of multiple conjugation in the molecules of the cyclic salts (IIa-c), absorption bands appeared at a longer wave region of the spectrum (305-333 nm) in addition to the absorption bands of the benzene ring (Table 1).

The cyclic salts (Va-d) gave no depression of melting point with authentic samples from [2].

EXPERIMENTAL

The IR spectra were obtained on a UR 20 spectrometer in KBr disks or in Nujol. The UV spectra were obtained on a Specord UV-Vis spectrophotometer in ethanol. The purity of salts (IIa-c) was established by TLC on Silufol UV 254 plates in n-butanol–ethanol–water–acetic acid, 8:2:3:1, visualizing with iodine vapor.

The initial p-bis(3-dialkylamino-1-propynyl)benzenes were obtained according to [3, 4].

TABLE 4. Characteristics of the Initial Compounds (Ia-c), (IIa-c), and (IVa-d)

Compound	Empirical formula	Found, %		Calculated, %		Compound	Found, %	
		N	Br	N	Br		N	Br
Ia	$C_{22}H_{30}Br_2N_2$	6,01	33,62	5,81	33,19	IIa*	6,12	33,56
Ib	$C_{28}H_{38}Br_2N_2$	5,13	28,72	4,98	28,46	IIb	5,15	28,69
Ic	$C_{26}H_{34}Br_2N_2O_2$	5,15	28,32	4,94	28,09	IIc	5,19	28,38
IVa	$C_{22}H_{26}Br_2N_2$	5,44	33,72	5,86	33,47			
IVb	$C_{26}H_{30}Br_2N_2$	5,45	29,92	5,28	30,19			
IVc	$C_{28}H_{34}Br_2N_2$	5,34	28,79	5,02	28,67			
IVd	$C_{26}H_{30}Br_2N_2O_2$	5,09	28,32	4,98	28,47			

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*Compounds (Ia-c) and (IIa-c) are isomers.

TABLE 5. Elemental Analysis of Amines (VI)-(IX) and p-Bis(2-allyl-3-oxopropenyl)benzene 2,4-Dinitrophenylhydrazone

Compound	Empirical formula	Found, % / Calculated, %		
		C	H	N
VI	$C_{16}H_{20}N_2$	80,17 80,00	8,11 8,33	12,28 11,67
VII	$C_{20}H_{24}N_2$	81,94 82,19	8,41 8,22	9,24 9,59
VIII	$C_{22}H_{28}N_2$	81,67 82,50	9,26 8,75	8,48 8,75
IX	$C_{20}H_{24}N_2O_2$	73,44 74,07	7,67 7,41	8,50 8,64
2, 4-Dinitrophenylhydrazone of compound (III)	$C_{30}H_{26}N_8O_8$	57,75 57,51	4,30 4,15	17,22 17,89

Salts (Ia-c) and (IVa-d) were obtained by the reaction of the appropriate amine with allyl or propargyl bromide in absolute benzene. Yields were almost quantitative. Salts (Ia-c), (IIa-c), (IVa-d), and m-bis(3-dialkylamino-1-propynyl)benzenes (VI)-(IX) are described for the first time.

The physicochemical characteristics of compounds (Ia-c), cyclic (IIa-c), (IVa-c), cyclic (Va-d) salts, and amines (VI)-(IX) are given in Tables 1-3.

Data of elemental analysis for N and Br⁻ of the salts mentioned and for C and H of the amines (VI)-(IX) and of p-bis(2-allyl-3-oxopropenyl)benzene 2,4-dinitrophenylhydrazone corresponded to calculated values.

General Procedure for the Reaction of Salts (Ia-c) with Aqueous Alkali. A solution of KOH (1.9 N, 3.6 ml) was added gradually to a homogeneous solution of the initial salt (Ia-c) (5.3 mmole) in water (3-4 ml) (molar ratio salt–base was 1:0.8). The solution was heated at 80-85°C for 6 h. The reaction mixture was then extracted with ether [amine (12-18%) was detected in the ether extract by titration]. The ether extract was washed with hydrochloric acid. The acid layer was separated from the ether and was evaporated to dryness under vacuum. The obtained hydrochlorides of the various secondary bases gave no depression of melting point with authentic samples. The ether layer was dried over $MgSO_4$ and the ether distilled off. Oily carbonyl compound (III) (0.4-0.5 g) was obtained, which decomposed on distillation in vacuum. Its 2,4-dinitrophenylhydrazone had mp 166°C. Absorption bands were detected in the IR spectrum of compound (III) for a monosubstituted C=C bond at 940, 980, and 1640, a p-substituted benzene ring at 840, an aromatic ring at 1600, and an aldehyde group at 1719 and 2740 cm^{-1}.

A portion of the cyclic salt (IIa-c) separated from the aqueous solution of the reaction mixture on storage at room temperature and was separated by filtration. The mother liquor was acidified with hydrobromic acid and the water distilled off at low pressure. The organic salt was extracted from the dry residue with absolute ethanol. The cyclic salts were very poorly soluble in absolute ethanol, consequently they are isolated as a mixture with inorganic salt on filtration. Salts (IIa-c) were isolated from these mixtures by recrystallization from water. After distilling off the alcohol a dark colored salt (1.5 mmole approx.) was obtained and rapidly solidified in the air. Absorption bands for a doubly substituted C≡C bond at 2240 were absent from the IR spectra of these salts but absorption bands were present for an aromatic ring at 1600, a p-substituted benzene ring at 850, a monosubstituted C=C at 910, 930, 1640, and 3090, and also an absorption band at 1940 cm^{-1} with a low intensity characteristic of an allenic group.

The cyclization of m-bis[3-dialkyl(2-propynyl)ammonio-1-propynl]benzene dibromide (IVa-d) was carried out according to [2]. The cyclic salts (Va-d) gave no depression of melting point with authentic samples from [2].

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