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SYNTHESIS AND STRUCTURE OF DI-N-ARYLPYRROLO[1,2-*c*;5,6-*c*]CYCLOOCTANES

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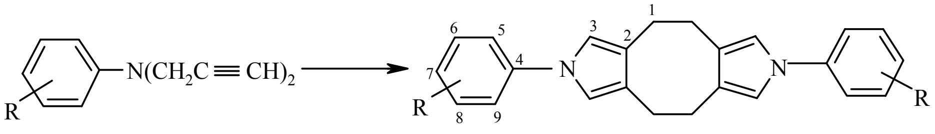
Di-N-arylpyrrolo[1,2-c;5,6-c]cyclooctanes were synthesized for the first time by the cyclization of N,N-dipropynylarylamines in a superbasic medium.

Keywords: di-N-arylpyrrolo[1,2-*c*;5,6-*c*]cyclooctanes, N,N-dipropynylarylamine, superbasic medium, cyclization.

The aim of the present work was to study the transformations of dialkynylarylamines in superbasic media.

By the cyclization of acetylene-containing compounds it is possible to obtain heterocyclic compounds with various structures [1, 2]. Use of the so-called "superbasic media" for this purpose opens up new prospects [3]. By superbasic we mean media consisting of a strong base and a solvent or reagent capable of binding specifically with a cation, "baring" anion [4, 5]. Such systems can be produced on the basis of linear ethers, crown ethers, dipolar aprotic solvents (DMSO, sulfolane, HMPA, etc.), amides, liquid ammonia, amines, and so forth.

We established that N,N-dipropynylarylamines **1a-d** are readily transformed at room temperature in a superbasic medium (DMSO, potassium hydroxide) into polycyclic compounds having various structures with 100% conversion [6-11]. Some of them were isolated from the reaction mixtures in the individual form on account of their low solubility in various solvents and their relative stability. On the basis of data from elemental analysis, IR and ^{1}H and ^{13}C NMR spectroscopy, and mass spectrometry (Tables 1-4) the isolated compounds were assigned the structure of di-N-arylpyrrolo[1,2-*c*;5,6-*c*]cyclooctanes **2a-d**.



1a–d **2a–d**

1, 2 a R = H, **b** R = *p*-Cl, **c** R = *m*-Cl, **d** R = *m*-Br

According to elemental analysis, the obtained compounds were isomeric with the initial N,N-dipropynylarylamines **1a-d**. According to mass spectrometry they were dimers giving a set of molecular ions corresponding to the isotopic composition of the halogen substituents (Cl, Br) [6].

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TABLE 1. The Physicochemical Characteristics of the Di-N-arylpyrrolo-[1,2-*c*;5,6-*c*]cyclooctanes **2a-d**

Compound	Empirical formula (*M*)	Found, % Calculated, %				mp, C*	R_f*2	Yield, %*3	
		C	H	Hal	N			A	B
2a	$C_{24}H_{22}N$ (338.45)	85.14 85.17	6.54 6.55	—	8.31 8.28	256-258	0.7	30	
2b	$C_{24}H_{20}Cl_2N_2$ (407.34)	70.46 70.77	5.08 4.95	17.67 17.41	6.74 6.88	302-304	0.6	47	10
2c	$C_{24}H_{20}Cl_2N_2$ (407.34)	70.94 70.77	5.33 4.95	17.41 17.41	6.87 6.88	179-180	0.6	40	10
2d	$C_{24}H_{20}Br_2N_2$ (496.28)	57.98 57.08	4.38 4.06	32.09 32.20	5.87 5.65	202-205	0.8	45	15

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* Crystallized from benzene (**2a**), xylene (**2b**), acetone–methanol (**2c**), and isopropanol–DMSO (**2d**).

*2 Silufol, benzene–petroleum ether 3:1 (**2a**), 1:1 (**2b**,**c**), and 2:1 (**2d**).

*3 DMSO–potassium hydroxide (A), HMPA–ether–potassium hydroxide (B).

The IR spectra of compounds **2a-d** do not contain the absorption band for the stretching vibrations of the ≡C–H bond at 3300 cm^{-1} characteristic of the initial alkynylamines **1a-d**, but new bands of medium or higher intensity characteristic of the stretching vibrations of the pyrrole ring appear in the region of 1380-1560 cm^{-1} [13]. The absorption bands for the stretching vibrations of the C=C bonds of the aryl substituents at 1500 and 1600 cm^{-1} remain [14].

Comparison of the experimental ^{1}H and ^{13}C NMR spectra with those calculated by means of the ChemOffice 4.5 Ultra software makes it possible to conclude that the experimental values of the resonance signals are close to those predicted for the structures of the di-N-arylpyrrolocyclooctanes **2a-d** (Tables 3 and 4). In fact, only one singlet for the vinyl proton in the region of 6.6-7.0 ppm with overall integral intensity corresponding to four protons, as in the calculated spectra for the protons of the pyrrole rings (6.41 ppm), is observed in the experimental ^{1}H NMR spectra. The chemical shift of the singlet for the methylene group in the region of 2.7-2.9 ppm coincides with the calculated chemical shift for the methylene groups of the cyclooctane ring at 2.70 ppm. The overall integral intensity of the multiplets for the aryl protons in the experimental spectra

TABLE 2. The Spectral Characteristics of the Cyclooctanes **2a-d**

Compound	M^+	IR spectrum (KBr), ν, cm^{-1}			
		C–Hal	C=C (arom.)	C=C–N (pyrr.)	C–H (arom.)
2a	—	—	1500, 1695	1530, 1 560 1380, 1400	3050, 3130
2b	404-409	775	1500, 1600	1527, 1550 1380, 1400	3030, 3090
2c	404-409	780	1500, 1603	1533, 1380, 1440	3070, 3130
2d	492-498	690	1490, 1590	1530, 1389, 1389, 1395	3065

corresponds to 8-10 protons, while the form depends on the type of substitution of the aryl ring and remains the same as in the initial arylamines **1a-d**. This indicates that the aryl rings are not affected during cyclization. A similar pattern is observed in the ^{13}C NMR spectra of the cyclic compounds **1a**,**c**. The chemical shifts of the C(1), C(2), and C(3) atoms in the experimental spectra, where the assignment of the signals was made by recording the single-resonance spectra from the protons, practically coincide with those calculated for the structures of the dipyrrolocyclooctanes **2a**,**c** (Table 4).

If the isomerization of the amines **1b-d** is conducted in 1:2 HMPA–diethyl ether, the yield of the respective cyclic dimers **2b-d** decreases to 0-15% even if the amount of potassium hydroxide is increased to 3 mole equivalents. The amine **1a** and N,N-dipropynyl-*p*-bromoaniline do not isomerize under these conditions, and N,N-dipropynyl-*p*-bromoaniline does not form the corresponding dipyrrolocyclooctane even during isomerization in the DMSO, potassium hydroxide medium.

The initial N,N-dipropynylarylamines **1a-d** were synthesized with yields of 80-90% by the procedures that we developed earlier from the corresponding arylamines and propargyl bromide on aluminum oxide [15] or in methanol solution in the presence of sodium acetate [16].

We have thus established that N,N-dipropargylarylamines **1a-d** cyclodimerize under superbasic conditions (DMSO, potassium hydroxide) at room temperature with the formation of the corresponding di-N-arylpyrrolo[1,2-*c*;5,6-*c*]cyclooctanes **2a-d**.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 spectrometer (300 MHz for ^{1}H, 75 MHz for ^{13}C) and a Tesla BS-487A spectrometer (80 MHz for ^{1}H) at 80°C. The melting points of the obtained compounds were determined on a Boetius heating bench (heating rate 4 deg/min). The IR spectra were obtained on a UR-20 spectrometer (in potassium bromide), and the mass spectra were obtained on an MX-1331 instrument with ionizing electron energy 60-70 eV.

TABLE 3. The ^{1}H NMR Spectra of Di-N-arylpyrrolo[1,2-*c*;5,6-*c*]-cyclooctanes **2a-d**

Compound	Spectrum	Solvent, (T, °C)	Chemical shifts, δ, ppm		
			N–CH=	–CH$_2$-	Ar
2a	Exp.	CDCl$_3$	6.85 (4H, s)	2.85 (8H, s)	7.11-7.39 (10H, m)
	Calc.*		6.41	2.70	7.3
2b	Exp.	DMSO -d$_6$ (~20)	7.03 (4H, s)	2.69 (8H, s)	7.34-7.45 (8H, m)
	Calc.		6.41	2.70	7.20-7.30
2c	Exp.	CDCl$_3$	6.65 (4H, s)	2.72 (8H, s)	7.00-7.20 (8H, m)
	Exp.	DMSO -d$_6$ (~20)	7.14 (4H, s)	2.75 (8H, s)	7.17-7.30 (8H, m)
	Calc.		6.41	2.70	7.10-7.30
2d	Exp.	DMSO-d$_6$ (80)	7.00 (4H, s)	2.75 (8H, s)	7.30-7.60 (8H, m)
	Calc.		6.41	2.70	7.20-7.40

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* Calc. indicates spectra calculated by means of the ChemOffice 4.5 Ultra software.

TABLE 4. The ^{13}C NMR Spectra of Cyclooctanes **2a**,**c**

Com-pound	Spectrum*	Solvent	Chemical shifts, ppm (J, Hz)								
			C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)
2a	Expt.	$CDCl_3$	28.3	126.7	119.3	140.5	117.2	129.4	124.6	129.4	117.2
	ESS		28.3 (t, J = 124.5)	125.7 (s)	119.3 (d, J = 164.6)	140.5 (s)	117.2 (d, J = 177.6)	129.4 (dd, J^1 = 161.2, J^2 = 7.2)	124.6 (d, J = 163.7)	129.4 (dd., J^1 = 161.2, J^2 = 7.2)	117.2 (d, J = 177.6)
	Calc.		28.1	124.1	118.7	140.4	120.2	129.1	125.3	129.1	120.2
2c	Expt.	$CHCl_3$	28.0	127.0	117.1	141.7	119.4	135.2	124.4	130.3	117.1
	Expt.	DMSO-d_6	26.8	125.8	116.4	140.5	117.2	133.7	123.4	130.7	115.9
	ESS		26.8 (t, J = 127.0)	125.8 (s)	116.5 (d, J = 186.8)	140.5 (s)	117.2 (d, J = 167.2)	133.7 (s)	123.4 (d, J = 168.5)	130.7 (d, J = 164.9)	115.9 (d, J = 165.0)
	Calc.		28.1	124.1	118.7	141.8	120.6	134.4	125.7	130.5	118.3

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* ESS indicates the experimental single-resonance spectrum, Calc. indicates the spectra calculated by means of the ChemOffice 4.5 Ultra software.

Di-N-arylpyrrolo[1,2-*c*;5,6-*c*]cyclooctanes 2a-d (General Procedure). To powdered potassium hydroxide (0.05 mol) in freshly distilled dry DMSO (20 ml) while stirring we added a solution of the amine **1a-d** (0.01 mol) in dry DMSO (15 ml) in a stream of inert gas (argon, nitrogen). The reaction was monitored by TLC on Silufol in the benzene–petroleum ether system. When the initial amine **1a-d** had disappeared from the reaction mixture, which required between 0.5 and 1.5 h, the whole reaction mixture was poured into 2-5 times the volume of water saturated with sodium chloride, and the pH was brought to 5-6 with ammonium chloride until the precipitate coagulated. The precipitate was filtered off, washed several times with water, and dried over calcium chloride in a desiccator until the mass of the precipitate stopped changing. The whole precipitate was then treated with a small amount of absolute ether. The insoluble part was filtered off, and the product was recrystallized from a suitable solvent.

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