## 2a,4a-DIAZACYCLOPENTA[c,d]AZULENES

## V. A. Kovtunenko, K. G. Nazarenko, and A. M. Demchenko

A method of preparing 5-aryl-1,2-pentamethyleneimidazoles from O-methylcaprolactim and  $\alpha$ -aminoacetophenone hydrochlorides is described. It is shown that 1,2-tri-, -tetra-, and -pentamethyleneimidazoles and phenacyl bromide give the corresponding quaternary imidazolium salts, cyclization of which in the presence of base gives the previously unknown 5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[c,d]azulenes (IVa-i).

Derivatives of the 2a,4a-diazacyclopenta[c,d]azulene (I) system are unknown. For contribution of its 5,6,7,8-tetrahydro derivatives we chose the method of pyrrole ring synthesis based on cyclization of  $\alpha$ -methyl-N-phenacylcycloimmonium salts [1-3] first described by A. Chichibabin [4].

As starting materials we used the 1,2-tri- and -tetramethyleneimidazoles (IIa, b) previously obtained by us [5, 6] together with a series of unknown 5-aryl-1,2-pentamethyleneimidazoles (IIc-f) described in this work. The bases IIc-f are quite stable, colorless materials synthesized by us in 54-74% yields by condensation of O-methylcaprolactim and the corresponding  $\alpha$ -aminoacetophenones.



II-III a-d  $R^1$  - H, a n = 1, R - Cl,  $R^2$  - OMe; b n = 2, R -  $R^2$  - OMe; c n = 3, R - H,  $R^2$  - Me; d n = 3, R - OMe,  $R^2$  - H; Ile n = 3, R - Cl; IIf n = 3, R - Br; III.e n = 3, R - OMe,  $R^1$  - H,  $R^2$  - Br; III f n = 3, R - Cl,  $R^1$  - H,  $R^2$  - OMe; III.g n = 3, R -  $R^2$  - Cl,  $R^1$  - H,  $R^2$  - Br;

Compounds IIa-f are alkylated by  $\alpha$ -haloketones through refluxing in polar solvents (alcohol or acetone) readily forming colorless, crystalline substances whose structures can be assigned as the quaternary imidazolium salts (IIIa-g) from their spectroscopic properties (see Table 1). The IR spectra of these salts showed carbonyl stretching vibrations at 1680-1690 cm<sup>-1</sup> and methylene group stretching bands at 2940-3050 cm<sup>-1</sup>. The size of the saturated ring has almost no effect on the position of the bands. The PMR spectra of the smaller sized ring shows a low field shift of the methylene group signals, being most marked in going from n = 2 to n = 1. A similar change was also observed for the imidazole 4-H signal found in the region 7.64-8.05 ppm. The position of the two proton phenacyl methylene resonance (6.05-6.17 ppm) does not depend on the ring size.

When refluxing solutions of the quaternary phenacyl salts IIIa-g in water or alcohol in the presence of base (sodium ethylate, sodium hydroxide, sodium or potassium carbonate) only IIIc-g (the 1,2-pentamethyleneimidazoles) gave the desired products (IV). In the case of IIIa,b a mixture of different compounds was obtained, the PMR spectra of which (on unpurified samples) did not show signals for pyrrole derivatives. The best yields of cyclization products for salts IIIc-g were obtained using 5% aqueous sodium hydroxide solution. Under these conditions other phenacyl 1,2-pentamethyleneimidazole salts also underwent a similar reaction without preliminary purification. The 1,4-diaryl-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[c,d]azu-

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	% 'P	IsiY	73	78	73	68	80	79	76
		other protons	3,90 (3H, s, 0 <u>CH</u> 3)	3,83 (3H, s, OCH3), 3,90 (3H, s, OCH3)	2,43 (3H, s, CH <sub>3</sub> )	3,83 (3H, s, 0CH <sub>3</sub> )	3,84 (3H, s, 0CH <sub>3</sub> )	3,88 (3H, s, 0 <u>CH</u> 3)	1,82 (3H, d, CHCH <sub>3</sub> ), 6,73 (1H, q, CHCH <sub>3</sub> )
	, ð, ppm	H <sub>arom</sub>	7,667,72 dd (4H), 7,198,05 dd (4H)	7,117,19 dd (4H), 7,568,02 dd (4H)	7,497,98 dd (4H), 7,517,63 m (5H)	7,167,40 dd (4H), 7,608,10m (5H)	7,157,43 dd (4H), 7,848,02 dd (4H)	7,188,03 dd (4H), 7,547,66 dd (4H)	7,508,15 dd (4H), 7,557,68 dd (4H)
	ectrum,	4-H S	8,04	7,76	7,71	7,68	7,64	7,72	8,05
	PMR Sp	cocH <sub>2</sub> s	6,05	6,04	6,17	6,17	6,19	6,13	ļ
		N-CH2 1	4,57	4,13	4,22	4,18	4,21	4,19	4,19
		C(2)-CH2	3,21	2.97	3,14	3,14	3,16	3,14	3,20
		(CH <sub>2</sub> ) <sub>n</sub> br s	2,76 (2H)	1,96 (4H)	1,87 (6H)	1,85 (6H)	1,86 (6H)	1,83 (6H)	1,87 (6H)
	IR Spectrum,	cm <sup>-1</sup>	3460, 2910, 3080 (C-H), 1680 (C-O), 1595 (C-C)	28302950, 3050 (C-H), 1590 (C-C)	28202930, 3080 (C-H), 1680 (C-O), 1595 (C-C)	28202940, 3060 (C-H), 1685 (C-O), 1590 (C-C)	28302940, 3060 (C-H), 1690 (C-O), 1580 C-C)	28202950, 3050 (C-H), 1680	28302940, 3050 (C-H), 1595 (C-C) (C-O), 1595 (C-C)
or IIIa-g		mp, °C	246247	226227	247248	237238	241242	232233	208209
eters fo	8	<sup>2</sup> z	6,26	6,12	<u>6.59</u>	<u>6,35</u>	5,38	5.89	5.58 5,67
Param	ound, %	H	<u>4.52</u> 4.50	<u>5.49</u> 5,51	<u>5,92</u>	5,71	<u>4.48</u> 4,65	<u>4.94</u> 5,08	<u>4.61</u> 4,69
emical	٣	U U	<u>55.9</u> 56.3	<u>60.2</u> 60.4	<u>64.3</u> 64.9	62.1 62,6	<u>52.9</u> 53,1	<u>57.6</u> 58.1	<u>55.6</u> 55,9
E 1. Physicoche		Empirical formula	C <sub>21</sub> H <sub>20</sub> BrCIN <sub>2</sub> O <sub>2</sub>	C <sub>23</sub> H <sub>25</sub> BrN <sub>2</sub> O <sub>3</sub>	C <sub>23</sub> H <sub>25</sub> BrN <sub>2</sub> O	C <sub>23</sub> H <sub>25</sub> BrN <sub>2</sub> O <sub>2</sub>	C <sub>23</sub> H <sub>24</sub> Br <sub>2</sub> N <sub>2</sub> O <sub>2</sub>	C <sub>23</sub> H <sub>24</sub> BrCIN <sub>2</sub> O <sub>2</sub>	C <sub>23</sub> H <sub>23</sub> BrCl <sub>2</sub> N <sub>2</sub> O
TABL		Com-	IIIa	qIII	IIIc	PIII	IIIe	IIIf	gIII

- IVa-i	
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Parameters	
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LE	2. Physicoclicin	IICAI F AI											
	-	Ŭ	Found, % alculated,	~ %	mp, °C				PMR SF	bectrum,	ð, ppm		Yield %
	Empirical formula	U	I	z	(solvent)	6-and 7-CH₂, S	8-CH <sub>2</sub> S	s-CH <sub>2</sub> S	3-Н, S	2-H, S	H1 and 4-Ar	R, R <sup>2</sup>	
1	C <sub>23</sub> H <sub>22</sub> N <sub>2</sub>	84.2 84 6	6.79	8.58 8.58	123124 (benzene – hexane)'	2,00	2,90	3,74	6,96	6,75	7,147,42 (9H)	- 2,37 (3H)	87
	C <sub>23</sub> H <sub>22</sub> N <sub>2</sub> O	80.2 80.7	6.48 6.48	8.83 8,18	162164 (benzene – hexane)	2,07	2,89	3,72	6,98	6,75	6,927,43 (9H)	- 3,83 (3H)	70
	C <sub>24</sub> H <sub>24</sub> N <sub>2</sub> O	<u>80.3</u> 80,9	<u>6,79</u>	7,86	133135 (benzene)	2,02	2,89	3,75	6,97	6,70	6,897,43 (9H)	– 1,44 <sup>1</sup> (2H), 4,07q(3H)	67
	C <sub>23</sub> H <sub>22</sub> N <sub>2</sub> O	81.0 80,7	<u>6.36</u> 6,48	<u>8.03</u> 8,18	170172 (benzene)	1,93	2,79	3,68	7,22	6,89	7,027,50 (9H)	3,81 (3H) -	92
	C <sub>23</sub> H <sub>21</sub> CIN <sub>2</sub> O	73.4	<u>5.56</u>	7.45	165166 DMF	1,95	2,78	3,68	7,22	6,91	7,027,41 (8H)	3,81 (3H) -	73
	C <sub>23</sub> H <sub>21</sub> BrN <sub>2</sub> O	<u>65.7</u>	<u>4.96</u> 5,04	<u>6,67</u>	193194 (pyridine)	1,95	2,80	3,64	7,18	6,90	7,007,60 (8H)	3,83 (3H) _	87
	C <sub>23</sub> H <sub>21</sub> CIN <sub>2</sub> O	73.4 73,4	<u>5.53</u> 5,63	<u>7.29</u> 7,45	185186 (pyridine)	1,88	2,74	3,69	7,35	6,82	6,917,55 (8H)	3,76 (3H)	<b>8</b> 4
	C <sub>23</sub> H <sub>21</sub> BrN <sub>2</sub> O	65.7 65.7	<u>4.94</u> 5,04	<u>6.51</u> 6,67	186188 (benzene)	1,94	2,88	3,69	7,00	6,74	6,927,57 (8H)	3,83 (3H)	11
	C23H20CI2N2	<u>2.93</u> 6,93	5,10	7,09	199200 (benzenc)	1,73	2,34	4,00	7,08	1,93 (HE)	7,337,57 (8H)	1 1	62

\*2-Me group signal.

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Fig. 1. Electronic spectra of salt IIIc (--) and base IVa (--).

lenes (IVa-i) obtained from quaternary salts IIIc-g are light yellow, crystalline materials, comparatively stable under normal conditions (see Table 2). The PMR spectra of IVa-i show broad, high field absorptions for the 6- and 7-CH<sub>2</sub> groups at 1.7 and 2.0 ppm and singlet signals for the 8- and 5-CH<sub>2</sub> groups at 2.3-2.9 and 3.6-4.00 ppm respectively. Signals for the 8- and 5-CH<sub>2</sub> groups can be identified amongst other aromatic protons in the region 6.7-7.6 ppm. Comparison of the spectra of bases IVa-h with that of IVi permits assignments of the signals at 7.0-7.3 ppm to the imidazole 3-H and at higher field (6.7-6.9 ppm) to the pyrrole 2-H. In the IR spectra of IVa-h carbonyl group absorption is absent and the appearance of the spectrum in the 3000 cm<sup>-1</sup> area is considerably simplified, hence the band at 3060 cm<sup>-1</sup> in the quaternary salts IIIc-g can be assigned to stretching vibrations of the 8-CH<sub>2</sub>.



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IVa R - H, R^1 - H, R^2 - Me; IVb R - H, R^1 - H, R^2 - OMe; IVc R - H, R^1 - H, R^2 - OEt;
IVd R - OMe, R^1 - H, R^2 - H; IVe R - OMe, R^1 - H, R^2 - Cl; IV<sub>1</sub>f R - OMe, R^1 - H, R^2 - Br;
IV g R - Cl, R^1 - H, R^2 - OMe; IV h R - Br, R^1 - H, R^2 - OMe; IV<sub>1</sub>f R - Cl, R^1 - Me, R^2 - Cl
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The electronic spectrum of IVa-i shows one more band than the corresponding phenacyl salt (see Fig. 1).

With the exclusion of IVi, all of the bases IVa-g condense with p-dimethylaminobenzaldehyde in the presence of HCl (the Ehrlich test for a pyrrole ring). With acids, the bases give salts, the structure of which will be discussed at a later time.

## EXPERIMENTAL

IR spectra were recorded on a Pye Unicam SP3-300 instrument for KBr tablets. PMR spectra were recorded at 100.13 MHz on a Bruker WR-100 instrument with TMS internal standard. UV spectra were taken for  $5 \cdot 10^{-5}$  solutions in methanol on a specord UV-vis instrument. Monitoring of the purity of the compounds prepared was done on Silufol UV-254 TLC plates with chloroform-methanol (9:1) elution. The quoted, corrected melting points were determined on a Boetius block.

Compound IIa with mp 145°C was synthesized as reported in [5] and base IIb was obtained from the corresponding hydrochloride (mp 210°C) using method [7].  $\alpha$ -Aminoacetophenone hydrochlorides were prepared by a standard method [8].

**5-Phenyl-1,2-pentamethyleneimidazole (IIc).**  $\alpha$ -Aminoacetophenone hydrochloride (8.75 g, 50 mmole) and Omethylcaprolactim (7.0 g, 55 mmole) were mixed and the viscous mass formed was left at room temperature for 48 h. Ether (100 ml) was added to the reaction mixture which was stirred for 2 h. The precipitate was filtered, washed with ether, and dissolved in 0.1 N HCl (100 ml). The solution was refluxed for 2 h, cooled, and ammonia solution was added to pH 10. The precipitated IIc was filtered, washed with water, dried *in vacuo*, and crystallized from hexane to give product (67%) with mp 102°C. PMR spectrum (CDCl<sub>3</sub>): 1.82 (6H, m, CH<sub>2</sub><u>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.96 (2H, t, C<sub>(2)</sub>-CH<sub>2</sub>), 3.92 (2H, t, N-CH<sub>2</sub>), 6.87 (1H, s, 4-H), 7.24-7.49 ppm (5H, m, H<sub>arom</sub>).</u>

**5-(4'-Anisyl)-1,2-pentamethyleneimidazole (IId).** Obtained similarly to IIc. Crystallization from ether gave product (54%) with mp 125-126°C. PMR spectrum (DMSO-D<sub>6</sub>): 1.72 (6H, m,  $CH_2CH_2CH_2CH_2$ ), 2.86 (2H, t,  $C_2-CH_2$ ), 3.86 (2H, t,  $N-CH_2$ ), 6.66 (1H, s, 4-H), 7.02-7.23 (4H, dd,  $H_{arom}$ ), 3.79 ppm (3H, s,  $O-CH_3$ ).

**5-(4-Chlorophenyl)-1,2-pentamethyleneimidazole (IIe).** Obtained similarly to IIc. Crystallization from ether gave product (70%) with mp 122-123°C. PMR spectrum (DMSO-D<sub>6</sub>): 6.79 (1H, s, 4-H), 2.86 (2H, t,  $C_{(2)}$ -CH<sub>2</sub>), 1.74 (6H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.91 (2H, t, N-CH<sub>2</sub>), 7.33-7.53 ppm (4H, dd, H<sub>arom</sub>).

**5-(4-Bromophenyl)-1,2-pentamethyleneimidazole (IIf).** Obtained similarly to IIc. Crystallization from hexaneisopropanol (1:1) gave product (74%) with mp 118-119°C. PMR spectrum (DMSO-D<sub>6</sub>): 1.75 (6H, m,  $CH_2CH_2CH_2CH_2CH_2$ ), 2.86 (2H, t,  $C_{(2)}$ -CH<sub>2</sub>), 3.91 (2H, t, N-CH<sub>2</sub>), 6.79 (1H, s, 4-H), 7.27-7.77 ppm (4H, dd, H<sub>arom</sub>).

**3-(4-Methoxyphenacyl)-5-(4-chlorophenyl)-1,2-trimethyleneimidazolium Bromide (IIIa).** A mixture of isopropanol (50 ml), base IIa (0.71 g, 3.2 mmole), and 4-methoxyphenacyl bromide (0.75 g, 3.2 mmole) was refluxed for 1 h. After cooling, the precipitate was filtered and crystallized from a mixture of methanol-isopropanol (1:1) to give IIIa (1.7 g).

Salts IIIc-g were prepared similarly to IIIa. Salt IIIc was purified by recrystallization from acetone, the remainder from isopropanol.

The basic parameters for IIIa-g are given in Table 1.

1-(4-Tolyl)-4-phenyl-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[c,d]azulene (IVa). Salt IIIc (1.06 g, 2.5 mmole) was treated with 5% NaOH solution (150 ml) by refluxing for 1 h. After cooling, the precipitate was filtered, washed with water dried, and crystallized from benzene-heptane (1:1) to give IVa (0.71 g).

Bases IVd, f, g, i were obtained similarly to IVa.

1-(4-Anisyl)-4-phenyl-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[c,d]azulene (IVb). A mixture of base IIc (2.12 g, 10 mmole) and 4-methoxyphenacyl bromide (2.29 g, 10 mmole) in isopropanol (150 ml) was refluxed for 1 h and then for 15 min with the addition of activated charcoal. After filtering, the hot solution was evaporated *in vacuo*, 5% NaOH solution (150 ml) was added, and the product was refluxed for 1 h. The mixture was cooled and the precipitate filtered, washed with water, and dried. Crystallization from benzene – hexane (1:1) gave IVb (2.4 g).

Bases IVc,e,h were obtained similarly to IVb.

Parameters for IVa-i are given in Table 2.

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