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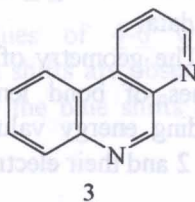
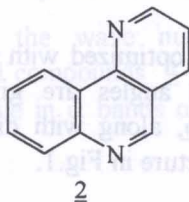
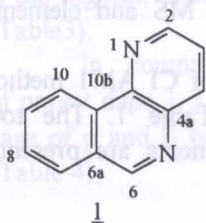
## QUATERNARY SALTS OF ISOMERIC 1,5-, 1,6- AND 4,6-DIAZAPHENANTHRENES WITH 1,2-DIBROMOETHANE

**Abstract:** The synthesis of quaternary salts of 1,5-, 1,6- and 4,6-diazaphenanthrenes with 1,2-dibromoethane is described along with their electronic structure and geometry optimization by CI AM1 method.

The UV spectra of the above salts have been compared with those of parent diazaphenanthrenes.

### Introduction

The present paper is a continuation of our research concerning 1,5-, 1,6- and 4,6-diazaphenanthrenes (dap) 1-3 and their derivatives. These compounds are interesting for reactivity<sup>1,2</sup> and physicochemical properties<sup>3,4</sup>; they show antibacterial, and in some cases antineoplastic activities.<sup>5-8</sup>

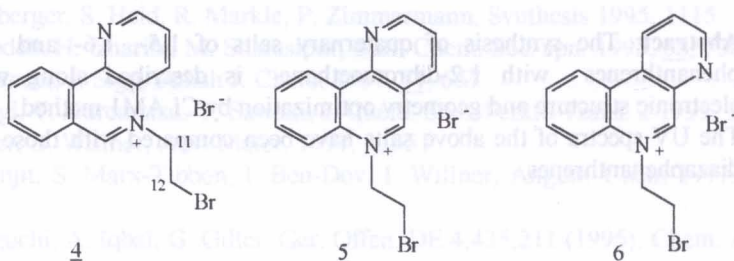


The presence of two nitrogen atoms in the dap molecule is responsible for their complexing properties<sup>9</sup> as well as formation of N - oxides<sup>10,11</sup> and quaternary salts.<sup>12</sup>

Quaternary salts of daps with iodomethane<sup>8</sup>, diiodomethane<sup>13</sup>, with phenacyl bromide and ethyl bromoacetate<sup>14</sup> as well as with allyl iodide and benzyl chloride<sup>7</sup> have been obtained and characterized. The salts of daps with phenacyl bromide and ethyl bromoacetate<sup>14</sup> are precursors of ylides, useful in 1,3-dipolar cycloaddition reactions.<sup>15,16</sup>

Quaternary salts of azaaromatics<sup>17</sup> are of interest as systems promising in the construction of electronic devices<sup>18</sup>, as model compounds for the investigation of biomimetic processes<sup>19</sup>, as dyes<sup>20</sup>, surfactants<sup>21</sup> and pharmaceuticals.<sup>22</sup> These compounds are usually obtained from parent azaaromatics in the quaternization reactions or from pyrylium salts by treatment with a primary amine<sup>17</sup>; in our experiments the first approach was used.

The present work deals with quaternary salts of 1,5-, 1,6- and 4,6-daps with 1,2-dibromoethane, i.e. 5-(2-bromoethyl)-1,5-diazaphenanthrene bromide 4, 6-(2-bromoethyl)-1,6-diazaphenanthrene bromide 5 and 6-(2-bromoethyl)-4,6-diazaphenanthrene bromide 6.



## Results and discussion

Reactions of daps with 1,2-dibromoethane have been performed in benzene medium using a 16-fold excess of the quaternizing agent; the yields of the obtained 4-6 range between 30.8 and 37.5%. The structure of 4-6 has been confirmed by <sup>1</sup>H NMR, MS and elemental analysis data.

The geometry of 4-6 was optimized with the use of CI AM1 method; the values of bond lengths and angles are given in Table 1. The total and binding energy values of 4-6, along with dipole moments are presented in Table 2 and their electronic structure in Fig.1.



The UV spectra of 4-6 have been recorded in 1,2-dichloroethane solution and compared with those of parent 1-3.<sup>23</sup> The experimental UV values are given in Table 3 and the differences between wavenumber values of 4-6 and those of 1-3 in Table 4. The UV spectrum of 4 is shown in Fig.2.

In quaternization of 1,5- and 1,6- daps with 1,2-dibromoethane the nitrogen atoms N5 and N6 are more reactive than those in 1 position due to steric reasons; the reactions lead to 4 and 5, respectively. This fact is in accordance with our earlier observations of higher reactivity of unshielded nitrogen atoms in other quaternization reactions of 1,5- and 1,6-daps<sup>7,14</sup> and in their N - oxidation.<sup>8</sup>

In the case of 4,6-dap both nitrogen atoms are similarly accessible, however only N6 undergoes quaternization with 1,2-dibromoethane affording 6; the same behaviour was found in reactions of 4,6-dap with diiodomethane<sup>13</sup>, phenacyl bromide<sup>15</sup> and ethyl bromoacetate.<sup>16</sup>

In the consideration of geometry of 4-6 optimized by CI AM1 method, in the cyclic system the highest discrepancies from the bond length and angle values usual to aromatic species are found in both azaaromatic rings, due to presence of nitrogen atoms. The longest bonds are to be found for C $\beta$ -C $\gamma$  positions and the shortest ones - for N-*tert* C $\alpha$  positions of pyridine rings. For 4-6 the highest angle values are for  $\alpha$  positions of pyridine rings; in 1 and 2 this angle is larger in the side azaaromatic ring than this in the middle one.

For the 2-bromoethyl group of 4-6, the bond length values are higher than for cyclic system, and increase in the order N-C11 < C11-C12 < C12 - Br.

In the electronic structure of 4-6, the highest effective charge values are found at positions  $\alpha$  and  $\gamma$  of pyridine rings and the lowest ones in  $\beta$  positions. The highest total energy value, i.e. the lowest stability is found in the case of 3, the sequence for total energy and binding energy values being 2 < 1 < 3.

The lowest core interaction energy was calculated for 3 and the highest for 2 isomer; the dipole moment values lie between 5.090 - 7.099D, the sequence is 4 < 5 < 6.

Having in view the experimental UV results of 4-6 it was observed that  $\log \epsilon$  of  $\alpha$  bands is lower than in the case of p and  $\beta$  bands, and  $\log \epsilon$  of  $\beta$  band is the highest, except for 5, where it is slightly lower than that of the p band (Table3).

In comparison of the wave number values of 4-6 with those of parent daps 1-3<sup>23</sup>, for all compounds 4-6 the red shifts are observed in the case of p and  $\beta$  bands, while in  $\alpha$  bands of 4 and 5 the blue shifts are found (Table 4).

The deshielding influence of 2-bromoethyl group is seen in  $^1\text{H}$  NMR spectra of **4**–**6** as compared with those of parent **1**–**3** daps; in **4** and **5** the signals of H6 and H5 as well as those of H4 and H7 are shifted downfield<sup>7</sup>; in **6** also the downfield shift of signals of H1 and H10 is observed<sup>16</sup>.

## Experimental

Melting points determined on Boetius apparatus are uncorrected. The progress of reactions has been watched with the use of tlc on 60F 254 silica gel (Merck) precoated DC aluminium sheets.

The  $^1\text{H}$  NMR spectra have been registered on the Varian 500 MHz spectrometer in  $(\text{CD})_3\text{SO}$  using  $\text{SiMe}_4$  as internal standard. The mass spectra have been made on LKB-2091 (70 eV) spectrometer.

The calculations have been made on IBM Pentium 166 computer, using Hyper Chem 4.5 program. The UV spectra have been recorded on the UV-vis Specord Zeiss-Jena spectrophotometer using 1,2-dichloroethane as a solvent ( $c=10^{-4}\text{M}$ ).

## Synthesis of **4**

To 1,5-dap (1.8g; 10 mmol) was added 1,2-dibromoethane (30 g; 160 mmol) and benzene (23 ml) and refluxed under dry conditions during 12 hours. The hot reaction mixture was treated with cold benzene (10 ml), and the formed product I was filtered.

The filtrate was treated with 1,2-dibromoethane (1 ml) and refluxed during 6h; the repetition of the above procedure gave the product II. The filtrate refluxed for the next 24 h gave the product III.

Combined products I–III have been purified by dissolving in ethanol and the precipitation of oily contaminations with the excess of ether. The solvent was removed under reduced pressure and the residue heated with *n*-heptane. After the removal of *n*-heptane the residue was treated with cold ether in order to dissolve the remaining 1,5-dap.

The product was filtered and washed with acetone to give 1.25 g (34.2% yield) of **4** as small, colourless crystals, m.p.  $215^\circ\text{C}$ . The eluent for tlc was benzene/MeOH (5:1); MS:  $m/z$  180 (1,5 dap; 65.0%); 28 ( $\text{CH}_2\text{CH}_2$ ; 17.5%).

$^1\text{H}$  NMR ( $\delta$ , ppm): 9.51 (s, 1H, H6); 9.11 (d, 1H,  $J_{10,9} = 8.3$  Hz; H10); 9.08 (dd, 1H,  $J_{2,3} = 4.4$  Hz;  $J_{2,4} = 1.5$  Hz; H2); 8.53 (dd, 1H,  $J_{4,3} = 8.3$  Hz;  $J_{4,2} = 1.5$  Hz; H4); 8.33 (d, 1H,  $J_{7,8} = 7.8$  Hz; H7); 8.07 (ddd, 1H,  $J_{8,7} = 7.8$  Hz;  $J_{8,9} = 7.3$  Hz;  $J_{8,10} = 1.5$  Hz; H8); 7.95 (ddd, 1H,  $J_{9,10} = 8.3$  Hz;  $J_{9,8} = 7.3$  Hz;  $J_{9,7} = 1.0$  Hz; H9); 7.87 (dd, 1H,  $J_{3,4} = 8.3$  Hz;  $J_{3,2} = 4.4$  Hz; H3); ca 2.5; overlapped with DMSO (4H,  $\text{CH}_2\text{CH}_2$ ).



$^{13}\text{C}$  NMR ( $\delta$ , ppm): 140.8 (C10b); 139.8 (C10a); 138.9 ((C6); 135.2 (C6a); 133.7 (C2); 132.7 (C4); 132.0 (C9); 130.2 (C7); 129.7 (C8); 126.5 (C10); 125.0 (C3); 124.9 (C4a); 57.5 ( $\text{N}^+\text{CH}_2$ ); 30.5 ( $\text{CH}_2\text{Br}$ )

For  $\text{C}_{14}\text{H}_{12}\text{N}_2\text{Br}_2$  (368.07): calcd. 45.69% C; 3.29% H; 7.61% N; found 45.46% C; 3.47% H; 7.88% N.

### Synthesis of 5

The reaction of 1,6-dap (1.8g; 10mmol) in a similar procedure afforded products I-III, which were combined and recrystallized from isopropyl alcohol to give 1.38 (37.5% yield) of **5** as small colourless crystals, m.p.  $236^\circ\text{C}$ ; MS:  $m/z$  180 (1,6dap; 92.5%); 28 ( $\text{CH}_2\text{CH}_2$ ; 24.0 %).

$^1\text{H}$  NMR ( $\delta$ , ppm): 9.79 (s, 1H, H5); 9.38 (dd, 1H,  $J_{2,3} = 4.4$  Hz;  $J_{2,4} = 1.8$  Hz; H2); 9.15 (dd, 1H,  $J_{10,9} = 7.9$  Hz;  $J_{10,8} = 1.7$  Hz; H10); 8.86 (dd, 1H,  $J_{4,3} = 8.1$  Hz;  $J_{4,2} = 1.8$  Hz; H4); 8.27 (dd, 1H,  $J_{7,8} = 7.9$  Hz;  $J_{7,9} = 1.7$  Hz; H7); 8.05 (ddd, 1H,  $J_{8,7} = 7.9$  Hz;  $J_{8,9} = 7.1$  Hz;  $J_{8,10} = 1.7$  Hz; H8); 8.10-7.95 (m, 2H, H3, H9); ca 2.5; overlapped with DMSO (4H,  $\text{CH}_2\text{CH}_2$ ).

For  $\text{C}_{14}\text{H}_{12}\text{N}_2\text{Br}_2$  (368.07) calcd. 45.69% C; 3.29% H; 7.61% N; found 45.51% C; 3.35% H; 7.68% N.

### Synthesis of 6

Analogous reaction of 4,6 dap (1.8 g; 10 mmol) afforded products I-III, which were combined and dissolved in hot methanol and after cooling treated with ether in order to precipitate oily contaminations. The crystals formed were filtered. The recrystallization from *n*-heptane and then from THF/ $\text{Et}_2\text{O}$  (1:1) mixture afforded 1.13 g (30.8% yield) of **6** as colourless crystals, m.p.  $217^\circ\text{C}$ . MS:  $m/z$  180 (4,6 dap; 81.0 %); 28 ( $\text{CH}_2\text{CH}_2$ ; 14.5%).

$^1\text{H}$  NMR ( $\delta$ , ppm): 9.46 (s, 1H, H5); 9.32 (d, 1H,  $J_{1,2} = 8.2$  Hz; H1); 9.14 (dd, 1H,  $J_{3,2} = 4.4$  Hz;  $J_{3,1} = 1.5$  Hz; H3); 8.88 (dd, 1H,  $J_{10,9} = 7.3$  Hz;  $J_{10,8} = 1.5$  Hz; H10); 8.20 (ddd, 1H,  $J_{8,7} = 7.3$  Hz;  $J_{8,9} = 7.1$  Hz;  $J_{8,10} = 1.5$  Hz; H8); 8.06-7.83 (m, 3H, H2, H7, H9); ca 2.5; overlapped with DMSO (4H,  $\text{CH}_2\text{CH}_2$ ).

For  $\text{C}_{14}\text{H}_{12}\text{N}_2\text{Br}_2$  (368.07) calcd. 45.69% C; 3.29% H; 7.61% N; found 45.50% C; 3.51% H; 7.78% N.

Table 1

Bond lengths ( Å ) and angles ( ° ) for 4-6 calculated with CI AM1 method4

N1-C2	1.32788
C2-C3	1.42296
C3-C4	1.37806
C4-C4a	1.42652
C4a-N5	1.40999
N5-C6	1.33887
C6-C6a	1.42422
C6a-C7	1.41589
C7-C8	1.38087
C8-C9	1.40806
C9-C10	1.38711
C10-C10a	1.40805
C10a-C10b	1.45847
C10b-N1	1.36851
N5-C11	1.47036
C11-C12	1.52280
C12-Br13	1.91335
C4a-C10b	1.43632
C6a-C10a	1.41976
N1-C2-C3	123.476
C2-C3-C4	118.883
C3-C4-C4a	119.206
C4-C4a-C10b	118.024
C4a-C10b-N1	121.486
C10b-N1-C2	118.919
C4a-N5-C6	120.249
N5-C6-C6a	122.902
C6-C6a-C10a	119.573
C6a-C10a-C10b	117.938
C10a-C10b-C4a	119.299
C10b-C4a-N5	120.030
C6a-C7-C8	119.758
C7-C8-C9	120.179
C8-C9-C10	120.859
C9-C10-C10a	120.047
C10-C10a-C6a	119.013
C10a-C6a-C7	120.144
C4a-N5-C11	120.313
N5-C11-C12	113.352
C11-C12-Br13	110.894

5

N1-C2	1.33075
C2-C3	1.42789
C3-C4	1.37568
C4-C4a	1.42316
C4a-C5	1.41899
C5-N6	1.33920
N6-C6a	1.41505
C6a-C7	1.41897
C7-C8	1.38361
C8-C9	1.40336
C9-C10	1.38299
C10-C10a	1.41194
C10a-C10b	1.45153
C10b-N1	1.36977
N6-C11	1.47030
C11-C12	1.52273
C12-Br13	1.91403
C4a-C10b	1.42909
C6a-C10a	1.42793
N1-C2-C3	124.214
C2-C3-C4	118.501
C3-C4-C4a	118.739
C4-C4a-C10b	119.056
C4a-C10b-N1	121.388
C10b-N1-C2	118.103
C4a-C5-N6	122.745
C5-N6-C6a	120.495
N6-C6a-C10a	119.745
C6a-C10a-C10b	119.720
C10a-C10b-C4a	117.753
C10b-C4a-C5	119.521
C6a-C7-C8	120.235
C7-C8-C9	120.734
C8-C9-C10	120.057
C9-C10-C10a	120.840
C10-C10a-C6a	119.071
C10a-C6a-C7	119.053
C5-N6-C11	119.179
N6-C11-C12	113.473
C11-C12-Br13	110.741

6

C1-C2	1.37777
C2-C3	1.43077
C3-N4	1.32399
N4-C4a	1.37801
C4a-C5	1.44028
C5-N6	1.33548
N6-C6a	1.41407
C6a-C7	1.42060
C7-C8	1.38123
C8-C9	1.40523
C9-C10	1.38101
C10-C10a	1.41293
C10a-C10b	1.43767
C10b-C1	1.42144
N6-C11	1.47273
C11-C12	1.52232
C12-Br13	1.91436
C4a-C10b	1.42336
C6a-C10a	1.42881
C1-C2-C3	119.088
C2-C3-N4	123.536
C3-N4-C4a	117.315
N4-C4a-C10b	123.560
C4a-C10b-N1	117.041
C10b-C1-C2	119.459
C4a-C5-N6	122.335
C5-N6-C6a	120.938
N6-C6a-C10a	119.501
C6a-C10a-C10b	119.766
C10a-C10b-C4a	118.803
C10b-C4a-C5	118.632
C6a-C7-C8	120.269
C7-C8-C9	120.581
C8-C9-C10	120.030
C9-C10-C10a	121.270
C10-C10a-C6a	118.485
C10a-C6a-C7	119.348
C5-N6-C11	118.887
N6-C11-C12	113.454
C11-C12-Br13	110.717

Table 2

Total energy, core interaction energy, formation heat and dipole moment values for 4-6 calculated by CI AM1 method

	<u>4</u>	<u>5</u>	<u>6</u>
Total energy (eV)	-2717.96225	-2717.98164	-2717.89871
Binding energy (eV)	-131.75908	-131.77847	-131.69554
Core interaction energy (eV)	13806.57729	13807.13358	13804.93482
Formation heat (eV)	10.10636	10.08697	10.16990
$M_x/D$	-4.708	-2.224	1.152
$M_y/D$	-1.096	-5.288	-6.860
$M_z/D$	1.594	-1.739	-1.420
$M(M)/D$	5.090	5.995	7.099

Table 3

Experimental wavenumber and  $\log \epsilon$  values of 4-6 (in 1,2-dichloroethane,  $c=10^{-4}M$ )

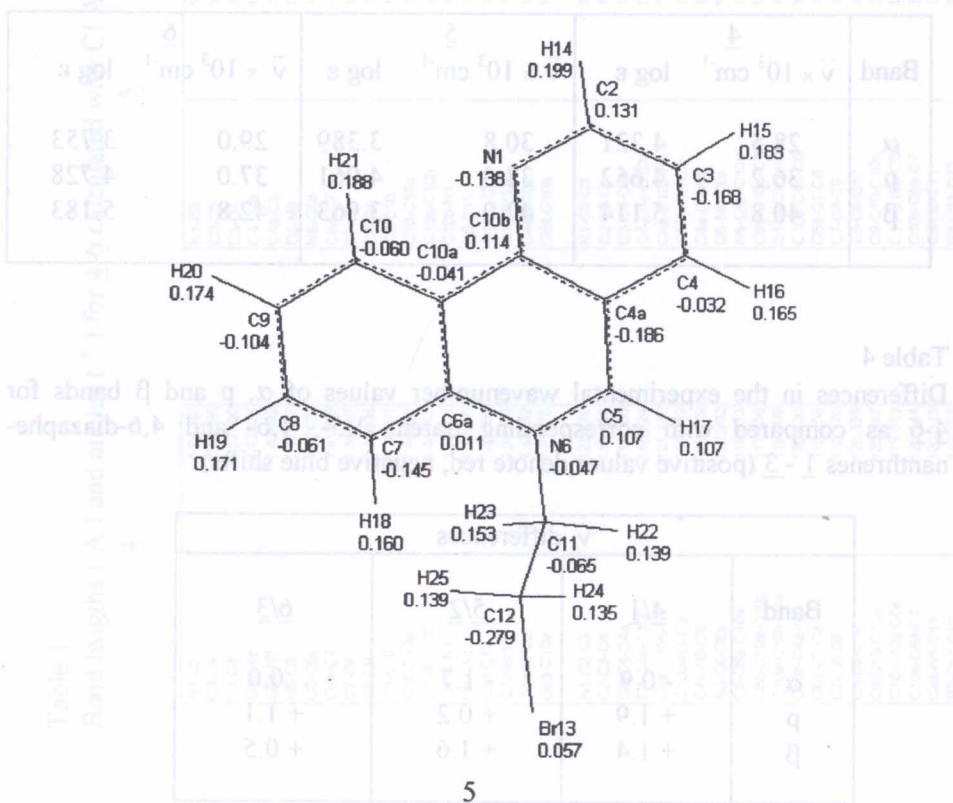
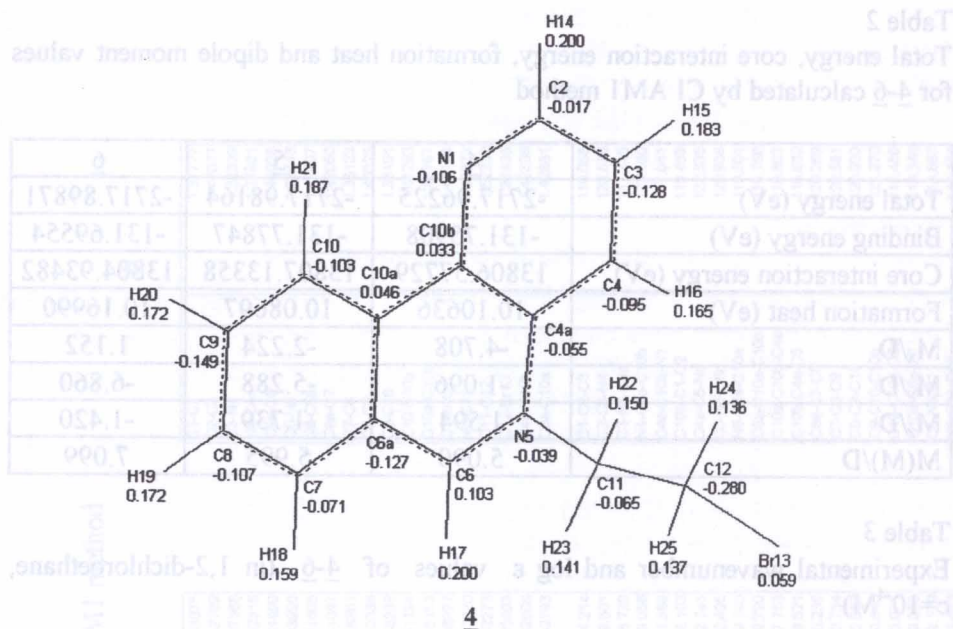
Band	<u>4</u>		<u>5</u>		<u>6</u>	
	$\bar{\nu} \times 10^3 \text{ cm}^{-1}$	$\log \epsilon$	$\bar{\nu} \times 10^3 \text{ cm}^{-1}$	$\log \epsilon$	$\bar{\nu} \times 10^3 \text{ cm}^{-1}$	$\log \epsilon$
$\alpha$	28.5	4.321	30.8	3.389	29.0	3.753
p	36.2	4.652	38.0	4.061	37.0	4.728
$\beta$	40.8	5.114	42.0	3.963	42.8	5.183

Table 4

Differences in the experimental wavenumber values of  $\alpha$ , p and  $\beta$  bands for 4-6 as compared with corresponding parent 1,5-, 1,6- and 4,6-diazaphenanthrenes 1-3 (positive values denote red, negative blue shifts)

Band	$\bar{\nu}$ differences		
	<u>4/1</u>	<u>5/2</u>	<u>6/3</u>
$\alpha$	-0.9	-1.7	0.0
p	+1.9	+0.2	+1.1
$\beta$	+1.4	+1.6	+0.5







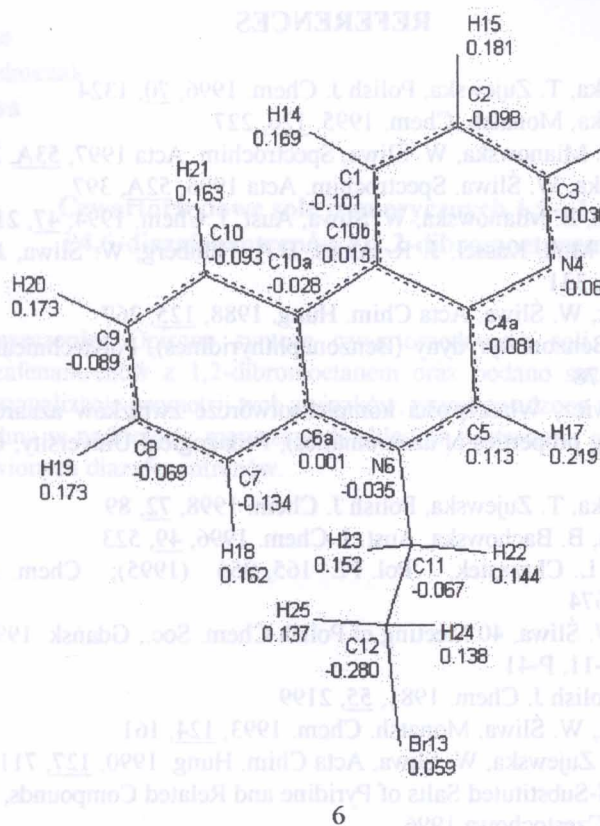


Fig. 1  
Effective charge values for **4-6** calculated with CI AM1 method

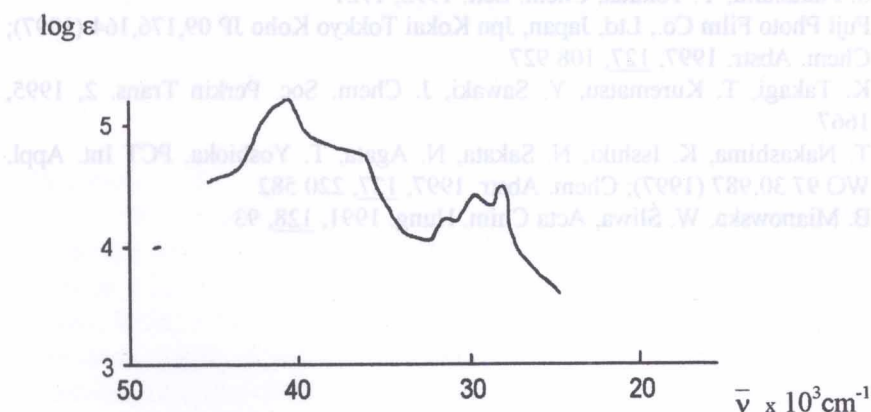


Fig. 2  
The experimental UV spectrum of **4**

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### Czwartorzędowe sole izomerycznych 1,5-, 1,6- i 4,6-diazafenantrenów z 1,2-dibromoetanem

**Streszczenie:** Opisano syntezę czwartorzędowych soli 1,5-, 1,6- i 4,6-diazafenantrenów z 1,2-dibromoetanem oraz podano strukturę elektronową i optymalizację geometrii tych związków, przeprowadzoną metodą CI AM1. Widma w nadfiolecie rozważanych układów porównano z widmami niepodstawionych diazafenantrenów.

### WPLYW POCHODNYCH TETRAZOLO- [2,1-c]CHINOKSALINY NA SKŁAD AMINOKWASOWY BIAŁKA NACIOWEGO

**Streszczenie:** W pracy doświadczalnej badano wpływ pochodnych tetrazolo-[2,1-c]chinoksaliny na skład aminokwasowy białka naciowego w łaciach selera naciowego w fazach wzrostu. Pod wpływem zaprogramowanych związków aromatycznych wystąpiły zmiany w składzie aminokwasowym białka. W całym okresie wegetacyjnym zaznaczył się wzrost poziomu takich aminokwasów jak: leucyna, fenylalanina, histydyna, leucyna, kwas asparaginowy i glutaminowy.

#### Wprowadzenie

W badaniach dotyczących wpływu środków ochrony roślin jako związków biologicznie czynnych, na wartość odżywczą roślin uprawnych, wiele miejsca poświęcono zmianom poziomu białka wywołanym przez te substancje (Bode, Wink, 1984; Bubicz, Nakarska, 1983; Czerwowska i in., 1981; Feireabend, Schubert, 1978; Fernandez-Pascual i in., 1983; Kashayap, Pandey, 1982; Kostkowska i in., 1984; Picozynski i in., 1990; Shah, Prathapasanan, 1992; Upadhyaya i in., 1985; Zwolińska-Smetalska, 1984). Coraz częściej prowadzone są analizy składu aminokwasowego białka roślinnego w celu określenia wartości biologicznej stosowanych preparatów (Bubicz,