Małgorzata Deska

Jan Długosz University, Institute of Chemistry and Environmental Protection,
42-201 Częstochowa, Armii Krajowej Ave 13/15, e-mail: m.deska@ajd.czest.pl

Calculations of reactivity of isomeric 1,5- , 1,6- and 4,6-diazaphenanthrenes

Abstract: Theoretical determination of the reactivity of isomeric 1,5-, 1,6- and 4,6-diazaphenanthrenes has been made by analysis of their thermodynamic stability as well as considering Fukui reactivity indices. Calculations have been performed by semiempirical AM1 method. Obtained results are compatible with experimental data.

Keywords: diazaphenanthrenes, effective charge, reactivity index, thermodynamic stability

Introduction

Isomeric 1,5-, 1,6- and 4,6-diazaphenanthrenes (dap) **1–3** and their derivatives are intensively studied due to their interesting reactivity [1,2] and biological activities [3] (Fig. 1). Reactions of daps afford their carbon and nitrogen substituted derivatives. To carbon substituted derivatives belong formyl- [4], methyl- [5], hydroxyethyl- [6,7], nitro- [3], amino- [8] and azo- [9] daps.
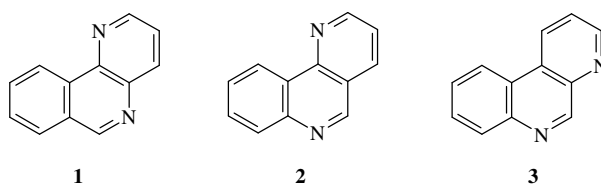

Figure 1. Formulas of 1,5-, 1,6- and 4,6-diazaphenanthrenes

Due to the presence of nitrogen atoms in the molecule, daps may be submitted to quaternization reaction leading to N-methyl- [10], N-ethyl- [11], N-haloalkyl- [12], N-ethoxycarbonyl- [13] and N-phenacyldaps [14], these both latter species being of interest as precursors of 1,3-dipoles in cycloaddition reactions [15, 16].

The presence of nitrogen atoms in the dap molecule besides quaternization reactions enables formation of their N-oxides [17] and complexes with transition metal ions [18]. One should mention also tetracyclic compounds obtained from daps [19, 20].

Having in view a variety of products synthesized from daps, the determination of their reactivity seems to be important. For calculations the semiempirical AM1 method has been chosen since its time of work is not so long as in the case of *ab initio* calculations.

Experimental

Calculations were made with full geometry optimalization on the Pentium III 733 MHz computer with two processors as well as on PC computer with a Pentium 266 MHz processor. For calculation of reactivity indices of **1–3** the AM1 method of the MOPAC 1993 program has been used. All stationary states have been optimized to the gradient norm 0.2 using EF procedure.

To take into account the solvent influence, additionally the COSMO algorithm (Conductor-like Screening Model), MOPAC 1993 has been applied [21]. The solvent in the COSMO method is simulated by its dielectric constant EPS, effective solvation radius R_{sol} and by the NSPA parameter determining the solvation density. Calculations have been made for temperature of 298, 318, 338, 358, 378 and 398K in the simulated presence of acetonitrile as a solvent; the EPS was taken as 37.5, for R_{sol} equal to 1A and for NSPA equal to 42.

Results and discussion

The considered **1–3** molecules have two nitrogen atoms as potential reactive centers, therefore the determination of differences in the reactivity of both N atoms is of interest; for this purpose the thermodynamic stability of corresponding forms was made and the calculated values have been compared with experimental results.

Generally the reactivity indices are classified into static and dynamic ones [22, 23]. According to Hammond postulate [24], for exothermic reactions the early transition state is important, *i.e.* the geometric and thermodynamic parameters of the transition state resemble starting materials, therefore in this case the static indices may be used for the reactivity determination.

On the other hand, for endothermic reactions the transition states are structurally similar to products, it is the case of the late transition state, and here dynamic reactivity indices are the most convenient (Fig. 2).
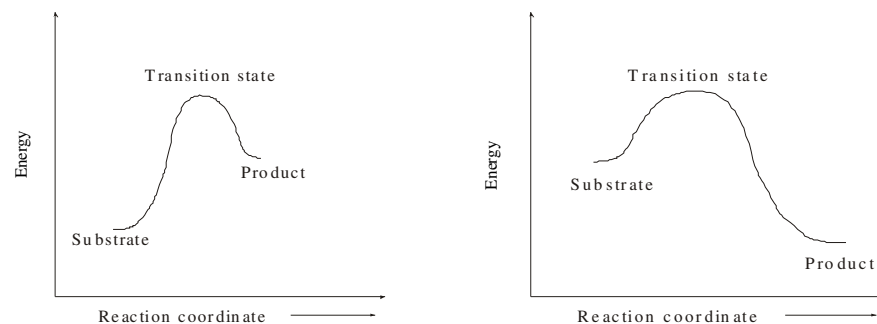
Figure 2. The plots of reaction energy for exothermic and endothermic steps

Since reactions of **1–3** with 2-haloethanol are endothermic, the reactivity of substrates was examined taking into account the thermodynamic analysis of products. Quaternization of **1–3** may theoretically occur on the nitrogen atom of the side or central ring, in each case affording two regioisomers (Fig. 3).

1,5-dap systems

I A   **I B**   **II A**   **II B**

1,6-dap systems

III A   **III B**   **IV A**   **IV B**
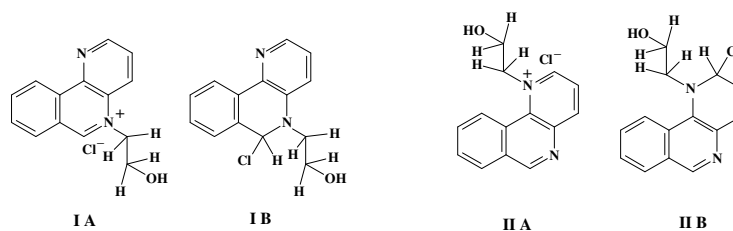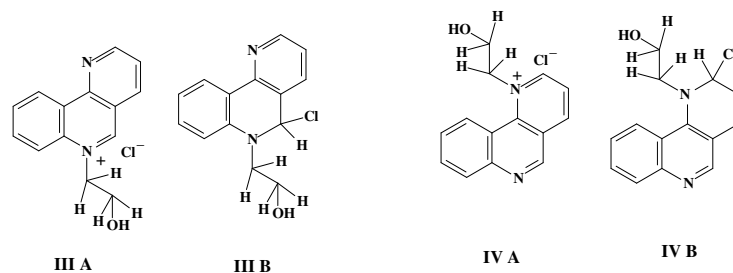
4,6-dap systems

Figure 3. Possible regioisomers formed in the reaction of **1–3** with 2-chloro-ethanol.

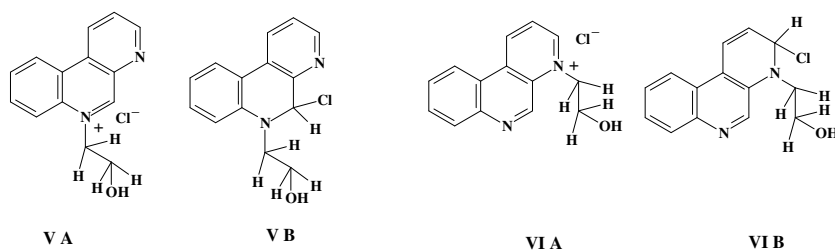The lower energy of formation of one from among two regioisomers indicates the higher probability of its formation, on the condition however that the process is under the thermodynamic control.

According to literature [25], the pyridinium salts may occur as the ionized form A, typical for aqueous solutions, or as the nonionized form B, prevailing in nonaqueous solutions, therefore the thermodynamic values of both theoretically possible regioisomeric forms have been calculated. The calculation results are given in Table 1.

Table 1 Thermodynamic properties of **1–3** derivatives I–VI

Compound	T, K	ΔH_T^0, kcal/mol	ΔS_T^0, cal/mol·K	ΔG_T^0, kcal/mol
I A	298	-3.083	105.1	-34.403
	318	-2.057	108.4	-36.528
	338	-0.960	111.8	-38.748
	358	0.206	115.1	-41.000
	378	1.441	118.5	-43.352
	398	2.743	121.8	-45.733
I B	298	-5.725	105.0	-37.015
	318	-4.678	108.4	-39.149
	338	-3.559	111.8	-41.347
	358	-2.369	115.2	-43.611
	378	-1.109	118.6	-45.940
	398	0.219	122.0	-48.337

Table 1. cont.

Compound	T, K	ΔH_T^0 , kcal/mol	ΔS_T^0 , cal/mol·K	ΔG_T^0 , kcal/mol
II A	298	-1.006	103.0	-31.700
	318	0.010	106.3	-33.793
	338	1.097	109.6	-35.948
	358	2.254	112.9	-38.164
	378	3.481	116.2	-40.443
	398	4.775	119.6	-42.826
II B	298	3.404	105.6	-28.065
	318	4.475	109.1	-30.219
	338	5.619	112.6	-32.440
	358	6.835	116.1	-34.729
	378	8.121	119.6	-37.088
	398	9.477	123.1	-39.517
III A	298	-3.960	103.4	-34.773
	318	-2.947	106.7	-36.878
	338	-1.863	110.0	-39.043
	358	-0.709	113.3	-41.270
	378	0.514	116.7	-43.599
	398	1.804	120.0	-45.956
III B	298	-5.736	104.1	-36.758
	318	-4.696	107.5	-38.881
	338	-3.585	110.9	-41.069
	358	-2.402	114.3	-43.321
	378	-1.150	117.7	-45.641
	398	0.172	121.1	-48.026
IV A	298	-1.125	102.9	-31.789
	318	-0.111	106.1	-33.851
	338	0.975	109.5	-36.036
	358	2.131	112.8	-38.251
	378	3.356	116.1	-40.530
	398	4.650	119.4	-42.871
IV B	298	2.275	107.0	-29.611
	318	3.357	110.5	-31.782
	338	4.511	114.0	-34.021
	358	5.736	117.6	-36.365
	378	7.032	121.1	-38.744
	398	8.379	124.6	-41.212

Table 1. cont.

Compound	T, K	ΔH_T^0 , kcal/mol	ΔS_T^0 , cal/mol ·K	ΔG_T^0 , kcal/mol
V A	298	-1.798	101.8	-32.134
	318	- 0.811	105.0	-34.201
	338	0.245	108.3	-36.360
	358	1.371	111.5	-38.546
	378	2.565	114.7	-40.792
	398	3.827	118.0	-43.137
V B	298	-6.734	101.6	-37.011
	318	-5.727	104.9	-39.083
	338	-4.644	108.2	-41.216
	358	-3.493	111.5	-43.410
	378	-2.272	114.8	-45.666
	398	-0.982	118.1	-47.986
VI A	298	-1.252	100.8	-31.290
	318	-0.298	103.4	-33.179
	338	0.727	107.0	-35.439
	358	1.820	110.2	-37.632
	378	2.981	113.3	-39.846
	398	4.208	116.5	-42.159
VI B	298	1.175	103.9	-29.211
	318	2.775	107.2	-31.315
	338	3.871	110.6	-33.512
	358	5.036	113.9	-35.740
	378	6.269	117.3	-38.070
	398	7.570	120.6	-40.429

When calculations for I–VI were made in the gaseous phase, the localization of ionized forms was impossible, in all cases only nonionized B forms have been obtained. However, when the solvent effect was taken into account, both ionized and nonionized forms could be localized.

For considered compounds, on the basis of Gibbs-Helmholtz equation (equation 1) and calculated by AM1/COSMO method the enthalpy ΔH_T^0 and entropy ΔS_T^0 values, the Gibbs energy ΔG_T^0 (Table 1) has been determined.

$$\Delta G_T^0 = \Delta H_T^0 - T \Delta S_T^0 \tag{1}$$

The standard thermodynamic potentials Δg_T^0 of the A → B conversion for I – VI have been obtained from the difference between Gibbs energy values of A and B (equation 2).

$$\Delta g_T^0 \;=\; \Delta G_T^0 \text{ (B)} \;-\; \Delta G_T^0 \text{ (A)} \tag{2}$$

Then using vant'Hoff equation (3), the thermodynamic pressure equilibrium constants K_{ap} were calculated (Table 2).

$$K_{ap} \;=\; \exp\left[\frac{-\Delta g_T^0}{R \cdot T}\right] \tag{3}$$

Table 2. Standard thermodynamic potential values Δg_T^0 and thermodynamic pressure equilibrium constants K_{ap} for the A → B conversion of I–VI

T (K)	Δg_T^0 (kcal/mol)	K_{ap}	Δg_T^0 (kcal/mol)	K_{ap}
	IA ⇌ IB		IIA ⇌ IIB	
298	-2.612	82.37016	3.635	0.00216
318	-2.621	63.30925	3.575	0.00349
338	-2.599	47.93416	3.508	0.00539
358	-2.611	39.27179	3.435	0.00800
378	-2.588	31.36452	3.355	0.01148
398	-2.604	26.91704	3.309	0.01523
	IIIA ⇌ IIIB		IVA ⇌ IVB	
298	-1.985	28.56914	2.178	0.02527
318	-2.003	23.80691	2.069	0.03784
338	-2.026	20.42275	2.015	0.04977
358	-2.051	17.87256	1.887	0.07046
378	-2.042	15.16105	1.786	0.09275
398	-2.070	13.70165	1.659	0.12273

Table 2. cont.

T (K)	Δg_T^0 (kcal/mol)	K_{ap}	Δg_T^0 (kcal/mol)	K_{ap}
	V A $\rightleftharpoons$ V B		VI A $\rightleftharpoons$ VI B	
298	-4.877	$37.76008 \cdot 10^2$	2.079	0.02986
318	-4.882	$22.67247 \cdot 10^2$	1.864	0.05234
338	-4.856	$13.80815 \cdot 10^2$	1.927	0.05674
358	-4.864	$9.32380 \cdot 10^2$	1.892	0.06997
378	-4.874	$6.58042 \cdot 10^2$	1.776	0.09399
398	-4.849	$4.60155 \cdot 10^2$	1.730	0.11219

The analysis of values from the Table 2 has shown that the conversion of A form into B is possible only in the case of I, III and V molecules, this fact being confirmed by a rather high K_{ap} constant values for these conversions. With higher temperature, the decrease of the K_{ap} values is observed.

The comparison of I, III and V with II, IV and VI, respectively, using data of the Table 1, shows that the ionized forms are energetically favored in the case of II, IV and VI, while nonionized ones in the case of I, III and V.

The calculated values correlate well with experimental results. However it should be noted, that they are true only in the case of reactions under thermodynamic control.

When the reaction is under kinetic control, the reactivity of substrates should be studied by static reactivity indices. The susceptibility for electrophilic substitution may be characterized for each molecule position by its electron density [26].

To explain the direction of quaternization of **1–3**, the Fukui reactivity indices for electrophilic substitution, occurring on nitrogen atoms have been calculated.

The reactivity index, proposed by Fukui is based on the statement that the frontier orbitals of reagents interact mainly in reactions and that the electron density on the frontier orbitals in the reaction center [27-29] is a crucial factor of the reactivity of the given position in the molecule.

For the reaction with electrophile, the index called the frontier electron density, *i.e.* the f_r^E index, may be calculated from the equation (4).

$$f_r^E = 2\,C_r^{\;2} \qquad\qquad (4)$$

C_r is the coefficient determining the contribution of atomic orbital in the molecular orbital on the r atom.

The calculated reactivity indices for electrophilic substitution of **1–3** are given in the Table 3. The higher frontier electron density f_r^E on nitrogen atoms at 5 and 6 positions shows the higher reactivity of nitrogen atoms in these positions as compared to that at 1 and 4 positions. These results are in accordance with experimental data.

Table 3. Fukui reactivity indices calculated for electrophilic substitution of **1–3**

Compound	Position	Fukui reactivity indices	
		in gas phase	in acetonitrile
1	N1	0.0002	0.0004
	N5	0.0640	0.0640
2	N1	0.0104	0.0134
	N6	0.174	0.1934
3	N4	0.0050	0.0154
	N6	0.0916	0.0776

A quite different approach to reactivity problem is given by analysis of effective charge values on particular atoms in molecule. The effective charge values in molecules may be obtained by taking into account not only the electron π charge, but also the charge of the atomic core [26]. The effective charge values [30] calculated by AM1 method, present on nitrogen atoms of **1–3** are given in the Table 4.

Table 4. The effective charge values of **1–3** calculated by AM1 method

Compound	Position	Effective charge
1	N1	-0.133
	N5	-0.125
2	N1	-0.140
	N6	-0.125
3	N4	-0.114
	N6	-0.125

Electrophiles are effective electron acceptors, and they attack positions of high electron density. The above calculations (Table 4) show that so for **1** as

for **2** the reactive position should be the N1 atom. This result does not agree with experimental data. In the case of **3**, however, the calculations are in accordance with experimental observations.

Conclusion

The above calculations have shown for **1–3** the highest reactivity of nitrogen atoms in 5 and 6 positions. This result was obtained so by analysis of thermodynamic stability of **1–3** as well as using Fukui reactivity indices. The calculation results correlate well with experimental data.

However, analysing effective charge values on nitrogen atoms of **1–3**, the compatibility of theoretical results with experimental data was achieved only for 3.

Concluding, it was shown that the orbital approach to the study of the reactivity of considered compounds gives better results than the analysis of effective charge values.

References

1.   W. Śliwa, *Current Org. Chem.*, 2003, **7**, 995.
2.   B. Bachowska and T. Zujewska, *ARKIVOC*, ***Part VI***, 2001, 77.
3.   L. Chrząstek, M. Mielniczak, Z. Staroniewicz and W. Śliwa, *Khim. Get. Soedin.,* 1999, 1396.
4.   J. Peszke, B. Mianowska and W. Śliwa, *Spectrochim. Acta*, 1997, **53A**, 2565.
5.   B. Mianowska and W. Śliwa, *Spectrochim. Acta*, 1996, **52A***,* 397.
6.   M. Deska and W. Śliwa, *Chem. Papers*, 2002, **56**, 309.
7.   B. Marciniak, V. Pavlyuk and M. Deska, *Acta Cryst.,* 2002, **E58**, 489.
8.   J. Peszke, L. Chrząstek and W. Śliwa, *Chem. Papers*, 2004, **58**, 176.
9.   L. Chrząstek and W. Śliwa, *Chem. Papers*, 2001, **55**, 42.
10. B. Dondela and W. Śliwa, *Khim. Get. Soedin.,* 2001, 944.
11. B. Marciniak, V. Pavlyuk and B. Dondela, *Acta Cryst.,* 2002, **E58**, 484.
12. J. Peszke and W. Śliwa, *Spectrochim. Acta*, 2002, **58A***,* 2127.
13. T. Girek, T. Zujewska and W. Śliwa, *Acta Chim. Hung.,* 1990, **127**, 711.
14. G. Matusiak and W. Śliwa, *Monatsh. Chem.*, 1993, **124**, 161.
15. G. Matusiak, *Aust. J. Chem.,* 1999, **52**, 149.
16. B. Bachowska and T. Zujewska, *Polish J. Chem.,* 1996, **70**, 1324.
17. T. Zujewska and B. Bachowska, *Polish J. Chem.,* 1998, **72**, 2507.
18. A. Gaudyn and W. Śliwa, *Chem. Papers*, 1994, **48**, 306.
19. W. Śliwa and M. Mielniczak, *Chem. Papers*, 1998, **52**, 747.
20. M. Paluszewski and W. Śliwa, PL 167956; (30.12.1995); *Chem. Abstr.,* 1996, *125*, 33641.
21. A. Klamt and G. Schüürmann, *J. Chem. Soc. Perkin Trans. II*, 1993, 799.
22. A. Gołębiewski, *Chemia kwantowa związków organicznych*, PWN, Warszawa 1973.

23. J. Sadlej, *Elementarne metody chemii kwantowej*, PWN, Warszawa 1966.
24. G.S. Hammond, *J. Am. Chem. Soc.,* 1955, **77**, 334.
25. J. Młochowski, *Chemia związków heterocyklicznych*, PWN, Warszawa 1994.
26. W. Kołos and J. Sadlej, *Atom i cząsteczka*, WNT, Warszawa 1998.
27. K. Fukui, *Topics Curr. Chem.*, 1970, **15**, 1.
28. I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, J.Wiley, London 1976.
29. M.T. Nguyen, A.K. Chandra, S. Sakai and K. Morokuma, *J. Org. Chem.,* 1999, **64**, 65.
30. J. Peszke and W. Śliwa, *Prace Naukowe WSP w Częstochowie,* Chemia IV, Częstochowa 1999, 145.

Małgorzata Deska

Obliczenia reaktywności izomerycznych 1,5-, 1,6- i 4,6-diazafenantrenów

Streszczenie: Teoretycznie oznaczono reaktywność izomerycznych 1,5-, 1,6- i 4,6-diazafenantrenów badając ich trwałość termodynamiczną, jak również stosując indeksy reaktywności Fukui. Obliczenia wykonano półempiryczną metodą AM1. Uzyskane wyniki są zgodne z wartościami doświadczalnymi.

Słowa kluczowe: diazafenantreny, ładunek efektywny, indeks reaktywności, trwałość termodynamiczna