Azo-Coupling Reactions Used in Analytical Chemistry: The Role of Reactants, Intermediates, and Aqueous Medium

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A quantum-chemical study of the analytically important azo-coupling reactions of naphthalen-1-amine (**1**) with naphthalene-1-diazonium (**2**) and 4-sulphobenzenediazonium (**8**) cations has been carried out. The reactions have been found to be frontier-controlled, and their regioselectivity is unequivocally determined by the thermodynamics of the intermediate σ-complexes, as well as by the aqueous medium. The latter defines high positional selectivity, providing the decision between two possible reaction routes predicted on the basis of quantum-chemical computations for separate molecular systems. As a result, azo coupling occurs at the 4- rather than at the 2-position of **1**. Furthermore, the aqueous medium makes the selection of analytical forms – protonated azo-coupling products with a quinonehydrazone-type structure.

1. Introduction. – The present theoretical work has been performed at the interface between different branches of chemistry and concerns azo-coupling reactions important for analytical sciences. The term 'analytical' is of chemical, not mathematical, meaning here. The terms 'analytical signal' and 'analytical form' are commonly accepted in analytical chemistry.

Azo coupling of aromatic amines and phenols with aryldiazonium cations (formed on diazotization of primary aromatic amines under the action of NO_2^- or nitroso compounds) are of great significance in dye production [1][2], as well as in analytical chemistry for the determination of NO_2^- (nitrite) [3][4] and nitroso species (including *N*-nitrosamines). The nitrite ion is toxic, an important environmental pollutant, and a precursor of *N*-nitrosamines possessing carcinogenic and mutagenic properties [5][6]. It interacts with oxyhemoglobin to form methemoglobin, which causes the disturbance of cellular respiration, and therefore, is of vital activity for the whole organism [7][8]. Nitrites are added to meat products to render a market appearance. Thus, the problem of nitrite and *N*-nitrosamine determination in foods is of great significance.

For nitrite and *N*-nitrosamine determination, the most-important and simplest method is photometry [3][4]. The following processes occur in photometric analysis (see *Schemes 1* and *2* below): *1*) auto coupling of naphthalen-1-amine (**1**) with naphthalene-1-diazonium (**2**) [3][4][9][10]; and *2*) *Griess* analytical reaction, *i.e.* sulphanilic acid diazotization and further azo coupling of the formed 4-sulfobenzenediazonium with **1** [3][4][11]. The former process occurs to only a small extent in aqueous solution, and the product precipitates [9][10]. However, the analytical-form yield and the analytical-signal stability with time become strongly enhanced, provided the reaction proceeds in 'microreactors' [12], *i.e.*, within micelles of an anionic

surfactant (*e.g.*, sodium dodecyl sulfate) [9][10]. In contrast, the *Griess* reaction works well in aqueous medium [3], and surfactant micelles improve the analytical signal only slightly (increase in the optical density of the analytical-form solution) and stabilize that with time [11].

Note that the analytical-signal stability and the thermodynamic stability of the molecular system discussed below are dissimilar concepts. The former is determined by a period during which the maximum intensity of the analytical signal remains practically unchanged, and the latter by the enthalpy and free energy of formation of a particular molecule. In a tandem of diazotization/azo coupling, the latter reaction plays a key role, since its products serve as a source for the analytical signal on photometric determinations of NO_2^- and *N*-nitrosamines.

According to *Parker* [13], the product of the auto-coupling of naphthalen-1-amine (**1**) is 4-amino-1,1′-azonaphthalene (**3**), resulting from substitution in 4-position (*Scheme 1*). Concurrently discussed in [13] is the possibility of triazene formation [13] by electrophilic attack of **2** at the N-atom of **1**. The *ortho*-coupled alternative product **4** was not reported by *Parker* [13]. However, a mixture of isomers with similar properties can, in fact, be generated, as found in the literature. For example, formation of the products of azo coupling *ortho* and *para* to the NH_2 group are known [1][14], including those for the azo components **1** and 2-methylnaphthalen-1-amine [14].

Zhukova and *Chekalin* [15] found the isomeric compounds **4** and **3** in yields of 8 and 92%, respectively, upon reaction of **2** with **1** in AcOH.

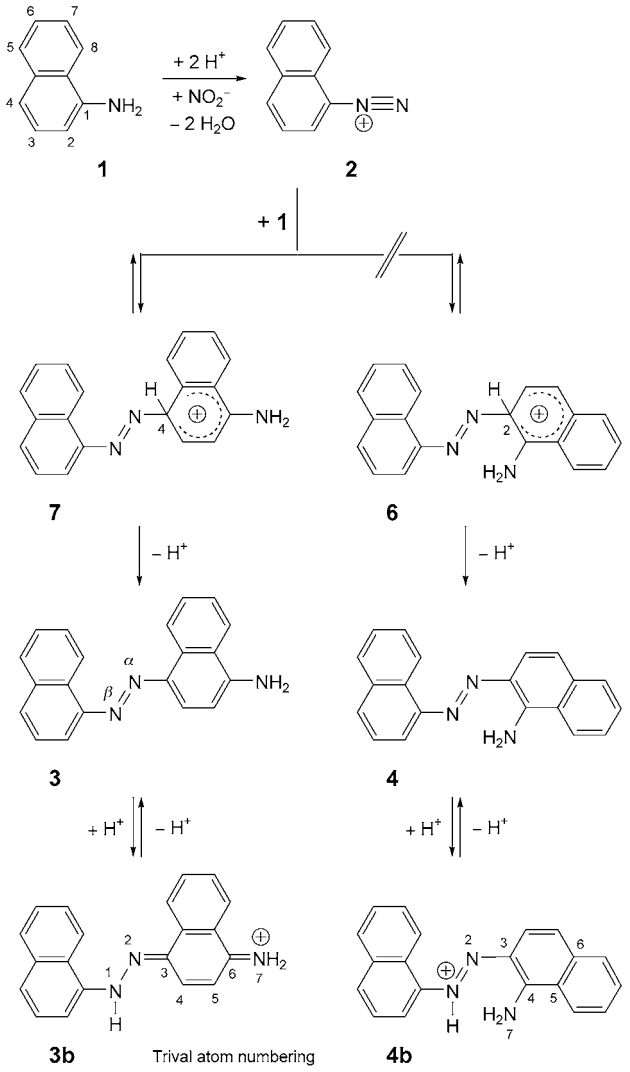
It is generally agreed [3][4] that the product of the *Griess* analytical reaction is 4-[(*E*)-(4-aminonaphthalen-1-yl)azo]benzenesulfonate (**5**) (see *Scheme 2* below). However, feasible is also the formation of the corresponding *ortho*-coupled isomer. Also, amino azo compounds – the products of both aforementioned analytical reactions – may undergo azo/quinonehydrazone tautomerism [16].

The processes of diazotization followed by azo coupling for analytical purposes occurs in acidic aqueous or micellar media. Therefore, the analytical forms must be *protonated* azo coupling products.

Quantum-chemical substantiation and prediction of the physicochemical properties and reactivities of diazo components (aryldiazonium cations) and azo constituents of the above reactions are of fundamental importance. We have already established [17–19] a number of various predictive quantitative structure/property relationships for a series of aryldiazonium compounds. The present work deals with aspects related to the chemical behavior of azo components, the structure and properties of analytical forms. The significance of quantum-chemical methods in the given case is increased because the isolation, purification, and identification of analytical forms existing solely in solutions would be impracticable.

2. Computational Methods. – PM3 Computations [20] were performed with the *MOPAC* package [21][22] under complete geometry optimization (*Broyden–Fletcher–Goldfarb–Shanno* function minimizer) [23], involving *Thiel*'s fast-minimization algorithm [24]. The preliminary optimization was realized by MMX molecular mechanics [25] with the *PCMODEL* software [25]. In quantum-chemical computations, the gradient norm was set not to exceed 0.02 kcal mol^{-1} $Å^{-1}$. In some cases, a sufficient decrease in gradient norm was achieved by abandoning *Thiel*'s fast minimization routine (the keyword 'NOTHIEL' of the MOPAC package was applied), or under optimization with the *Davidon–Fletcher–Powell* method (keyword 'DFP') [23], or by conducting double-precision calculations (keyword 'PRECISE'), as well as by means of combined approaches involving the keywords 'NOTHIEL', 'DFP', and 'PRECISE'.

Scheme 1. *Diazotization of Naphthalen-1-amine* (**1**) *Followed by Azo Coupling with the Resulting Diazonium Ion* **2**. Theoretically, the coupling can give rise to 2- or 4-substitution (products **4** *vs.* **3**, resp.), with different potential protonation sites.



Standard free energy values (ΔG_f were calculated from the relationship $\Delta G_f = \Delta H_f - T\Delta S_f$, where the standard entropies of formation (ΔS_f) were calculated as $\Delta S_f = S - \Sigma S_i$, and where S_i are the entropies of the elements constituting the molecules in their standard states [26], with hydrogen, nitrogen, oxygen, and sulfur being two-atomic molecules ($T = 298.15$ K).

The entropic contributions of separate degrees of freedom for translation, rotation, and vibration were computed in the rigid-molecule approximation (barriers of rotation and inversion much larger than kT), with no allowance for vibrational anharmonicity. The translation contributions were not calculated quantum chemically, and the rotation contributions relying on the data on equilibrium internuclear distances were obtained in the

course of quantum-chemical treatment. Finally, the contributions of vibrational components of entropy were evaluated on the basis of normal vibration frequencies computed by the quantum-chemical method. For computing the frequencies after geometry optimization, second-order derivatives of total energy by natural coordinates (force constants) were computed preliminarily [27].

In calculating the rotational contributions to thermodynamic functions, the symmetry number was taken as unity. For computing clusters of 101 H_2O molecules, the PM3 method was used within the *HyperChem* package *Hypercube, Inc.*, 1115 NW 4th Street, Gainesville, FL 32601, U.S.A.). Complete geometry optimization was carried out by means of the *Polak–Ribiere* conjugate gradient algorithm [23]. A minimal distance of 1.7 Å was assumed between the solute and H_2O molecules. Finally, log*P* calculations[1]) were performed by means of *HyperChem* within an additivity scheme using atomic parameters [28–31].

3. Results and Discussion. – The molecular systems studied in this paper, especially H_2O-containing clusters, are rather large. That is why sophisticated *ab initio* or DFT computations are not appropriate. On the other hand, for the series of compounds belonging to different classes and possessing various functional groups, we have established the correctness of the most-important thermodynamic and molecular characteristics generated by the MNDO, AM1, and PM3 methods [17–19][32–47], as well as of electronegativity, inductive and mesomeric parameters of atomic groups [48][49]. The PM3 method usually provides suitable results in obtaining the heats of formation of organic species [20][22]. Among the mentioned methods, PM3 is the only one that both provides realistic standard heats of formations for *cis* and *trans* azobenzenes, and reproduces correctly the sign of difference between standard heats of formation of the above isomers [18].

3.1. *Reaction of Naphthalen-1-amine* (**1**) *with the Naphthalene-1-diazonium Cation* (**2**). Diazonium formation and azo coupling between **1** and **2** are shown in *Scheme 1*. Azo couplings are electrophilic aromatic substitution reactions proceeding *via* σ-complex formation [50–53], *e.g.*, **6** and **7** in *Scheme 1*. Electrophilic attack of the cation **2** is, in principle, feasible at different positions of **1**.

In accordance with the HSAB (*Hard and Soft Acid and Base*) principle [54–56], aromatic π-electronic systems are soft bases [51]. Aryldiazonium cations are grouped with soft acids [57][58]. Soft/soft interactions should be frontier-controlled [51][59]. In that case, the azo-coupling regioselectivity must be described with similar reactivity indices as the electron density in frontier HOMO[2]) orbitals, as confirmed by the correlations of aryldiazonium reduction potentials with electron affinities [17–19].

The computed electron-density values of the frontier orbital of **1** (C(2), 0.143; C(3), 0.045; C(4), 0.189; C(5), 0.078; C(6), 0.027; C(7), 0.052; C(8), 0.068) show that azo coupling proceeds most likely *via* the C(4)-atom. Obviously, competing coupling could occur at C(2) (see *Scheme 1*). With allowance for some ambiguity in predicting the regioselectivity based on the HOMO electron density, for the restricted notions on charge and frontier control [59], we have overcome the framework of prereactive-state considerations from the viewpoint of analysis of static reactivity index, and simulated the barrier of the azo coupling of **1**. The energy of the σ-complex intermediate was assumed to be comparable to that of the transition state (localization approximation) [50][53][60]. The lesser the σ-adduct energy, the lower the activation energy of the process [60].

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[1]) '*P*' stands for 'partition coefficient' (octanol/H_2O system).

[2]) Highest-occupied molecular orbital.

Table 1 shows that the azo coupling with **1** proceeds at positions 2 and 4. Among the possible geometric coupling isomers, only the *trans* forms act as analytical-signal sources, since the *cis* isomers are nonplanar, lacking a contiguous chain of conjugation required for a sufficiently high band intensity in electronic absorption spectra. Therefore, the analytical forms of the azo coupling between **1** and **2** are compounds **3** and **4** (*Scheme 1*).

Table 1. *Thermodynamic Characteristics of the* trans-*Configured σ-Complexes, Presumably Formed on Electrophilic Attack by* **2** *of C- and N-Atoms at Different Positions of Molecule* **1**

Position	ΔH_f [kcal mol^{-1}]	S [cal mol^{-1} K^{-1}]	ΔG_f [kcal mol^{-1}]
2	288	141	349
3	313	135	376
4	288	136	351
5	302	139	364
6	313	143	373
7	303	137	365
8	312	137	374
N	302	136	365

Assuming kinetic control of azo coupling [51–53], and taking into account a fairly high activation barrier for triazene formation as a result of electrophilic attack of **1** by a N-atom (*Table 1*), this type of side product can be neglected. Moreover, the analytically active reaction product cannot be a triazene compound, which is nonplanar, lacking conjugation between the two naphthyl π-electronic systems. Actually, conjugation is even impossible in a planar triazene structure, since the NH group is an 'insulator' [61–68].

Because diazotization and azo coupling are performed in aqueous and micellar media at pH 3.0 [7–9], the reaction products exist in the form of their conjugate acids. Compounds **4** and **3**, respectively, can be protonated *a*) at the primary (p) NH_2 group, *b*) at the N_α-atom, or *c*) at the N_β-atom of the azo group (*Table 2*).

The location of the protonation site is not evident, although the NH_2 group is more basic than the azo N-atoms [52]. The explanation is that, as the bond order at the azo

Table 2. *Notation of the Cationic Conjugate Acids of the Azo-Reaction Products* **4** *and* **3**. The structures of **4b** and **3b** are shown in *Schemes 1* and *2*, respectively, those of the other protonated systems are not explicitly drawn (see text).

Azo compound	Protonation site[a])	Molecular system
4	α	**4a**
	β	**4b**
	p	**4c**
3	α	**3a**
	β	**3b**
	p	**3c**

[a]) The term 'p' stands for 'primary' amino group (NH_2).

group increases, its unshared electron pair occupies an orbital more and more similar to an s orbital [52]. Such an electron pair is displaced closer toward the N-nucleus, is confined by it more strongly, and becomes, therefore, less available to form a bond with a proton, leading to a decrease in the compound's basicity [52]. Contrary, however, upon protonation of the azo group, the positive charge can be delocalized over the π bonds. Finally, it cannot be predicted *a priori* how hydration will influence the protolytic properties of the system.

Table 3 contains a comparison of the thermodynamic stabilities of the cations **3a**–**c** and **4a**–**c**, as calculated according to the PM3 method, with an explicit account for aqueous medium. For this purpose, clusters involving the above cations and 101 H_2O molecules were considered. Analogously to [69–72], the distribution density for H_2O molecules in the cluster was close to that for its liquid state, *i.e.*, realistic aqueous solutions were simulated. An example of such a cluster is presented in the *Figure*.

Among the conjugate acids of **3** and **4**, the cations **3b** and **4b**, formed on protonation of the β-N-atom of the azo group, proved to be the most stable (*Table 3*).

For evaluating the probability of occurrence, as the analytical form of the auto coupling of **1** of either aminoazonaphthalene of two possible, the data from [9][10] were referred to. The azo-compound precipitate obtained when the reaction proceeded

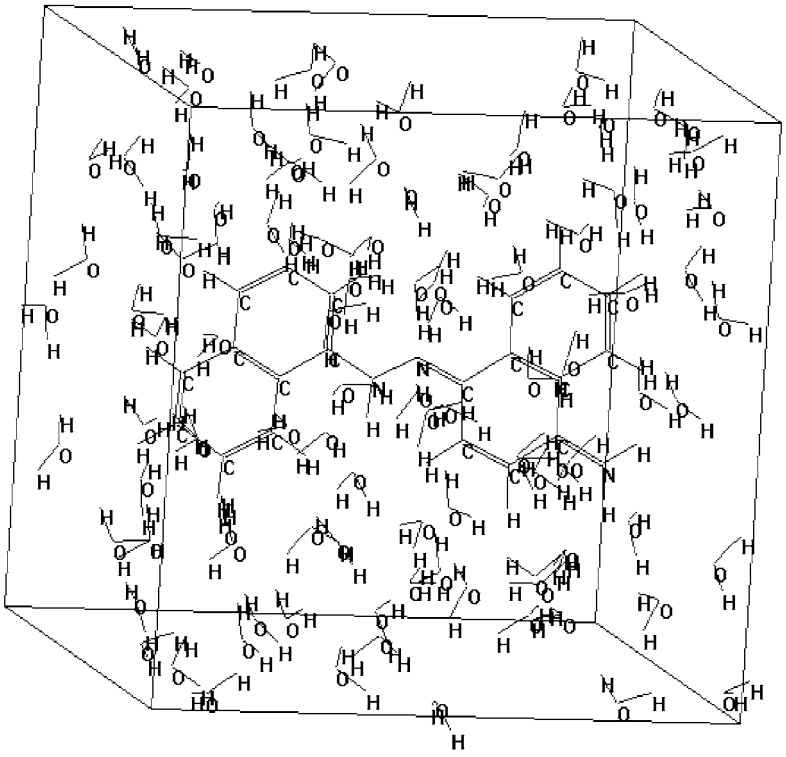


Figure. *Cluster containing the cation* **3b** *and 101* H_2O *molecules*

Table 3. *Differential Heats of Formation for Protonated Reaction Products of Type* **3** *and* **4** (see *Table 2*). $\Delta\Delta H_f = \Delta H_f(A \cdot 101\ H_2O) - \Delta H_f(B \cdot 101\ H_2O)$.

A	B	$\Delta\Delta H_f$ [kcal mol^{-1}]
3c	**3b**	53
3c	**3a**	42
3b	**3a**	– 11
4c	**4b**	29
4c	**4a**	12
4b	**4a**	– 17

in aqueous medium was isolated in a preparative manner [9][10]. An absorption band at λ_{max} 480 nm of a strongly alkaline solution of the isolated amino azo compound is typical for the nonprotonated azo form [15][16][73]. In strongly acidic and micellar media, λ_{max} 560 nm [9][10] corresponds to the quinonehydrazone form [16].

In accordance with our quantum-chemical computations, the tautomeric equilibrium for the nonprotonated compounds **3** and **4** in aqueous solution, indeed, is on the side of the azo forms, the $\Delta\Delta H_f$ values of the hydrated azo *vs.* hydrazo tautomers being equal to – 29 kcal/mol.

In cation **4b**, the unshared electron pair of the NH_2 group is excluded from conjugation. As follows from the bonds orders (*Table 4*), **4b** exists mainly in the azo form. *N*(β)-Protonation should not influence essentially the spectral characteristics of **4b** since the chromophore remains practically unchanged when gaining a proton. The electronic absorption spectrum of **4b** must be similar to that for *trans*-azonaphthalene, to which the absorption bands at λ_{max} 449, 424, 397, 383, 277, 267, 222, and 213 nm (in cyclohexane) correspond [74]. In the electronic spectra of acidic aqueous and micellar solutions of the isolated aminoazonaphthalene, no absorption was observed within the diagnostic range of 370 – 450 nm [9][10]. Therefore, the chromophore of azonaphthalene inherent in **4b** is absent, which excludes the presence of **4** among the azo-coupling products.

Table 4. *Calculated Bond Orders for the Cations* **3b** *and* **4b**

Bond	**3b**	**4b**
C(1) – C(2)	1.55	1.77
C(2) – C(3)	1.29	1.08
C(3) – C(4)	1.23	1.44
C(4) – C(5)	1.57	1.24
C(4) – C(7)	–	1.00
C(5) – C(6)	1.22	1.30
C(6) – C(7)	1.40	–

A quinoid structure is characteristic for **3b**, which is preferable in energy. Thus, the analytical form of the product of the auto coupling of **1** in micellar media is *trans*-4-amino-1,1′-azonaphthalene (**3**) in the form of its conjugate acid **3b**.

The aqueous medium defines high positional selectivity, providing the decision between two possible routes of reaction, as predicted on the basis of gas-phase quantum-chemical computations. As a result, azo coupling occurs at the 4-position of **1**.

This is in agreement with the reported yields of the isomers **3** and **4** [15]. The choice of the azo-coupling route in *Scheme 1* is due to a greater stabilizing effect of the aqueous medium with respect to σ-complex **7** as compared to **6** ($\Delta\Delta H_f = 33$ kcal/mol). Aqueous and micellar media provide selection not only of the reaction route, but also of the protonated form of the azo-coupling product with quinonehydrazone structure.

As can be seen from *Table 5*, the thermodynamic stabilities of the isolated cations formed on protonation of **3** are very similar in the gas phase.

Table 5. *Calculated Thermodynamic Gas-Phase Characteristics of the Cationic Compounds* **3a**, **3b**, *and* **3c**. For structures, see *Table 2*, *Scheme 2*, and text.

Cation	ΔH_f [kcal mol^{-1}]	S [cal mol^{-1} K^{-1}]	ΔG_f [kcal mol^{-1}]
3a	280	134	343
3b	277	134	340
3c	279	136	341

3.2. *Reaction of Naphthalen-1-amine* (**1**) *with 4-Diazoniobenzenesulfonate* (**8**). For substantiating the structure of the analytical form resulting from the azo coupling between **1** and **8** (*Scheme 2*), we performed a quantum-chemical study analogous to the above system. Since the azo coupling of both **8** and **2** involve the same substrate, *i.e.*, **1**, the whole reasoning behind the regioselectivity related to the analysis of HOMO electron density remains valid. *Table 6* shows that the lowest energy barrier is related to the electrophilic attack at positions 2 and 4 of the naphthalene ring. Consequently, the possible products of the *Griess* reaction are 4-[(*E*)-(4-aminonaphthalen-1-yl)azo]benzenesulfonate (**5**) and its *ortho*-congener **9**[3]) (*Scheme 2*). The corresponding triazene is unlikely to be formed, as follows from both *Table 6* and the nonplanarity of the triazene molecule.

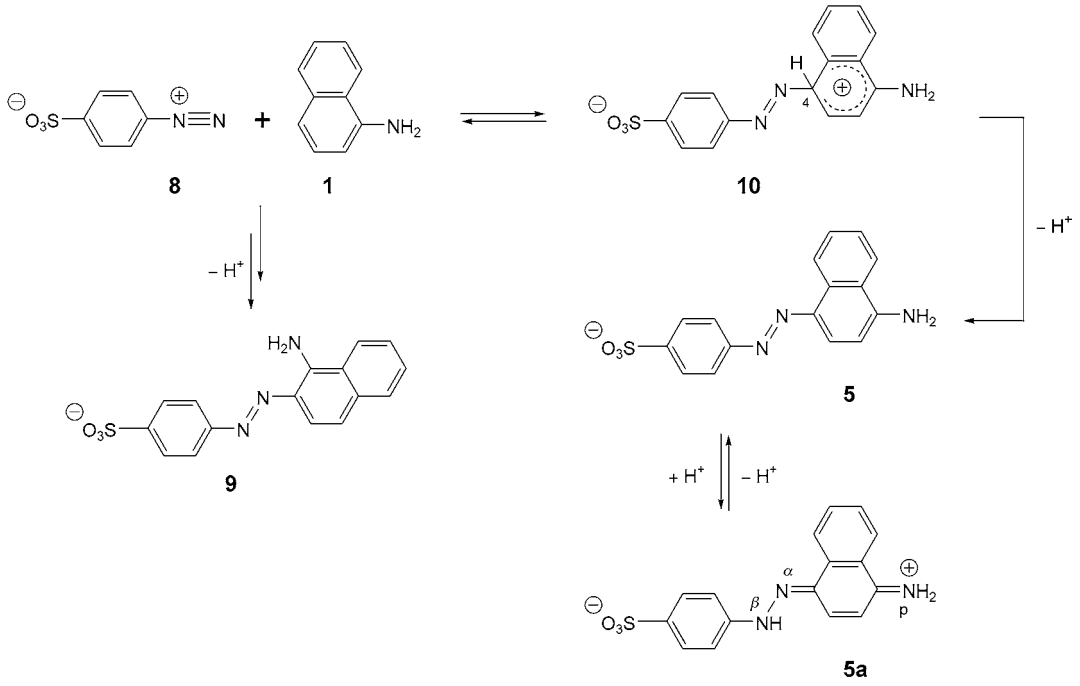
Table 6. *Thermodynamic Characteristics of* trans *σ-Complexes in the Azo-Coupling Reaction of* **1** *and* **8** (see *Scheme 2*)

Position	ΔH_f [kcal mol^{-1}]	S [cal mol^{-1} K^{-1}]	ΔG_f [kcal mol^{-1}]
2	157	147	220
3	180	146	252
4	155	158	223
5	170	148	241
6	181	147	253
7	170	158	238
8	178	157	239
N	168	150	239

Similar as for the auto-coupling products of **1**, the azo forms of nonprotonated **5** and **9** are most stable in aqueous solution. For **5**, ΔH_f (azo tautomer) $-\Delta H_f$ (hydrazo tautomer) is -70 kcal/mol in H_2O; in the case of compound **9**, the above difference between the heats of formation is -38 kcal/mol.

[3]) At a pH of 1–2 and higher [11], both compounds are in their anionic forms [75].

Scheme 2. *Azo Coupling of 4-Sulfobenzenediazonium* (**8**) *with Naphthalen-1-amine* (**1**)



Our quantum-chemical study shows that **5a**, the hydrazo form of β-*N*-protonated **5**, is the thermodynamically most-stable form in acidic H_2O (*Scheme 2*). The differential standard heats of formation of clusters containing, along with 101 H_2O molecules, the cations originating from protonation of the heteroatoms (α-N, β-N, p-NH_2) of **5**, are $\Delta H_f(p) - \Delta H_f(\beta) = 37$, $\Delta H_f(\beta) - \Delta H_f(\alpha) = -22$, and $\Delta H_f(p) - \Delta H_f(\alpha) = 15$ kcal/mol, respectively.

The electron-density distribution within **5a** confirms a quinoid structure, with bond orders for C(1)–C(2), C(2)–C(3), C(3)–C(4), C(4)–C(5), C(5)–C(6), and C(6)–C(7) of 1.47, 1.38, 1.18, 1.62, 1.18, and 1.46, respectively (atom numbering as for **3b** in *Scheme 1*).

Protonation of the azo compound **9** occurs preferably at the NH_2 group, without formation of a quinoid structure. For the different protonated forms of **9**, $\Delta H_f(p) - \Delta H_f(\beta)$ is -15, $\Delta H_f(\beta) - \Delta H_f(\alpha)$ is 10, and $\Delta H_f(p) - \Delta H_f(\alpha)$ is -5 kcal/mol, respectively.

The quinoid structure of the analytical form can be detected in the electronic absorption spectrum of the reactive system NO_2^-/**1**/sulphanilic acid/anionic surfactant [11], by a band at λ_{max} 550 nm [16]. Consequently, the analytical form of the *Griess* reaction is the cation **5a**. Similar to the case of the auto coupling of **1**, in the reaction of **1** with **8**, the aqueous medium is the decisive factor for the major product **5**. Thus, the σ-complex **10** is by 29 kcal/mol thermodynamically more stable as compared to the σ-complex preceding the azo compound **9** (not shown). The protonation site of **5** is also determined by the aqueous medium.

3.3. *Comparative Study of the Azo Coupling of* **1** *with Two Aryldiazonium Cations.* As follows from the aforesaid, the analytical forms fo the auto coupling of **1** and the *Griess* reaction are of analogous structure, which allows us to discuss different influences on the analytical signals characteristics for the processes mentioned. The azo coupling reactions were referred to as proceeding *via* formation of σ-complexes comparable, in terms of energy, to the transition states. A comparative estimation of activation barriers can be made from the values of dynamic reactivity index/cationic localization energy (Λ^+) [50][53] (*Table 7*), with $\Lambda^+ = \Delta H_f(\mathbf{1}) + \Delta H_f(R-N^+\equiv N) - \Delta H_f(\sigma\text{-complex})$ or $\Lambda^+ = \Delta G_f(\mathbf{1}) + \Delta G_f(R-N^+\equiv N) - \Delta G_f(\sigma\text{-complex})$.

Table 7. *Cationic Localization Energies on Forming the Intermediates of the Azo-Coupling Reactions of* **1** *with* **2** *or* **8**, *Respectively*

σ-Complex	Λ^+ [kcal/mol]	
	Enthalpy	Free energy
7	13.4	0.6
10	22.4	12.1

Electrophilic aromatic substitutions are kinetically controlled [51–53], which is why the lower the activation energy (*i.e.*, the higher the cationic localization energy), the higher the yield of the analytical form. For the azo coupling reaction of **1** and **8**, the cationic localization enthalpy and free energy are by 9 and 11.5 kcal/mol, respectively, higher than the corresponding values for the azo coupling of **1** and **8** (*Table 7*). Therefore, at the level of quantum-chemical computations for isolated molecular systems, the reaction between **1** and **8** is more favorable than that between **1** and **2** in aqueous medium. This explains the mentioned differences in the analytical-signal intensities of the reactions of **1** with **2** *vs.* **8** in aqueous solution [9–11]. Consequently, the results of comparative estimation of two azo-coupling reactions by the Λ^+ criterion are in compliance with the data obtained from the studies by electron-absorption spectroscopy [9–11].

Semiquantitative assessment of the solvent effect on the state of dissolved molecular systems (M) can be performed by the value ΔH_{aq}, characterizing the energy term of the interaction of a molecule M with a water-molecule ensemble, having a physical meaning of hydration enthalpy [69–72]: $\Delta H_{aq} = \Delta H_f(M \cdot mH_2O) - \Delta H_f(M) - \Delta H_f(m\ H_2O)$.

The hydration enthalpy of **5a** (−7.53 kcal/mol) is more negative than that of **3b** (+40.3 kcal/mol). Thus, aqueous media stabilize the analytical form **5a** of the *Griess* reaction to a greater extent compared to the product **3b** of the auto coupling of **1**. This result corroborates the data on the substantially higher stability with time observed for the analytical form of the *Griess* reaction in acidic aqueous solution, as compared to the auto-coupling product, which readily precipitates out of solution [9–11].

Let us now discuss a micellar-media effect on the analytical signal. The log*P* values [28–31] of **3b** and **5a** are 4.06 and 3.86, respectively. Since only the former is charged, it is concentrated by the anionic surfactant micelles to a greater extent than the electroneutral zwitter-ion **5a**. The log*P* values of the two species indicate high hydrophobicity. For comparison, note that hexane and octan-1-ol have log*P* values of

2.88 and 2.53, respectively, whereas MeOH and H_2O give rise to values of -0.27 and -0.51, respectively.

Computation patterns [28–31] for evaluating log*P* do not take into account charge. That is why the hydrophilic character of **3b** is underestimated. Hence, **3b** is probably more concentrated than **5a** in the outer polar hydrophilic component of the micelles. Thus, both aqueous (this work) and micellar [9–11] media stabilize, in a differential manner, the analytical forms of two reactions due to the differences in charge, hydrophobicity, and hydration of the azo compounds.

A combined analysis of charge effects and hydrophobicity of the reactive species [9–11] (according to [14][76] and references cited therein), of azo-coupling barriers, role of aqueous (this work) and micellar [9–11] media on the analytical forms enables one to rationalize the difference in the analytical-signal intensities for the reactions of **1** with two distinct aryldiazonium cations (**2** *vs.* **8**), as well as the difference in the analytical-signal intensities for each reaction in aqueous solution *vs.* surfactant micelles.

4. Conclusions. – The comparative studies in this work and in [9–11] of two model azo-coupling reactions with the same azo component (**1**) and in two different media (acidic aqueous solution *vs.* anionic-surfactant micelles) allowed us to formulate several regularities. Provided that the molecular systems of reactants and resulting substances are positively charged and rather hydrophobic, and the azo coupling activation energy is relatively high, then, in the presence of anionic surfactant [9][10], a considerable increase in the analytical-signal intensity in comparison to that of the aqueous solution occurs, as observed for the auto coupling of **1** (*Scheme 1*). When the reactants do not possess an overall positive charge, in the presence of hydrophilic atomic groups and at a lower activation energy of the azo-coupling process, the analytical reaction is straightforward even in aqueous medium [3][4][11]; in anionic surfactant micelles, the detection limit is diminished only slightly, and the analytical signal becomes more stable with time [11].

A set of factors enabling one to forecast the analytical effects on determining NO_2^- and nitroso compounds by means of azo coupling in aqueous and micellar media has been established, namely overall charge of molecular systems of reactants and analytical forms, cationic localization energy, hydration enthalpy, and log*P*. The regularities found could allow one to predict the reactivity, the analytical-form yield for the azo coupling with other azo and diazo components, and, finally, the comparative analytical characteristics of the reactions. For such predictions, it is necessary *i*) to identify differences in charge and hydrophobicity; *ii*) to estimate, by means of the appropriate quantum-chemical method, the activation energy of the reactions (cationic localization energy); *iii*) to perform the quantum-chemical evaluation of hydration enthalpies for reactions products, to compute log*P*; and *iv*) to consider the role of reactants and intermediates, as well as aqueous and micellar effects on the reactivity and the analytical signal.

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