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Reaction of *N*-Phenyl(benzylidene, phenoxy)acetyl-1,4-benzoquinone Imines with Sodium Azide

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Abstract—*N*-Phenyl(benzylidene, phenoxy)acetyl-1,4-benzoquinone imines reacted with sodium azide to give the corresponding 1,4-addition products, *N*-(4-hydroxyphenyl) carboxamides. Quantum chemical calculations showed that the initial step in the examined reaction is addition of azide ion to neutral quinone imine molecule.

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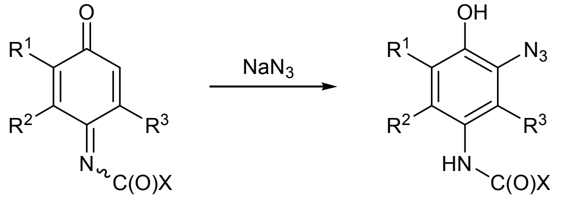
It was found previously that *N*-substituted 1,4-benzoquinone imines possessing at least one free *ortho* position with respect to the carbonyl carbon atom react with sodium azide according to the 1,4-addition pattern [1–5]. Products resulting from nucleophilic substitution of chlorine in positions *2* and *6* of the quinoid ring by azido group and 1,2-addition products were isolated only in the reactions with *N*-arylsulfonyl(acyl)-2,3,5,6-tetrachloro-(2,6-dichloro-3,5-dimethyl)-1,4-benzoquinone imines [2, 3]. The mechanism of this reaction was not studied previously.

In the present work we examined reactions of previously synthesized quinone imines **I**–**III** [6] with sodium azide at a reactant ratio of 1 : 2 and mechanism of the process. The reactions were carried out in acetic acid at room temperature (reaction time 1–2 h), and the products were exclusively azido-substituted amino phenols **IV**–**VI** formed as a result of 1,4-addition of azide ion (Scheme 1). The reactions with compounds **Ia**, **Ib**, **IIa**, **IIb**, and **IIIa**–**IIIc** were accompanied by reduction of the initial quinone imines.

Scheme 1.



Ia–**Ic**, **IIa**–**IIc**, **IIIa**–**IIIc** → **IVa**–**IVc**, **Va**–**Vc**, **VIa**–**VIc**

I, **IV**, X = PhCH=CH; **II**, **V**, X = $PhCH_2$; **III**, **VI**, X = $PhOCH_2$; $R^1 = R^2 = Me$, $R^3 = H$ (**a**); $R^1 = R^3 = Me$, $R^2 = H$ (**b**); $R^1 = H$, $R^2 = R^3 = Me$ (**c**).

In the ^1H NMR spectra of **IV**–**VI** we observed signals at δ 8.88–9.53 and 9.29–9.52 ppm due to NH and OH protons, respectively. Protons of the CH_2 and OCH_2 groups in **V** and **VI** gave singlets at δ 3.59–3.61 and 4.66–4.69 ppm, respectively, and signals from the CH=CH fragment of **IV** appeared as two doublets in the region δ 6.88–7.53 ppm. The IR spectra of **IV**–**VI** displayed a strong narrow peak in the region 2180–2110, which is typical of azido group, and absorption bands at 3350–3200 and 3430–3380 cm^{-1} due to stretching vibrations of the NH and OH groups.

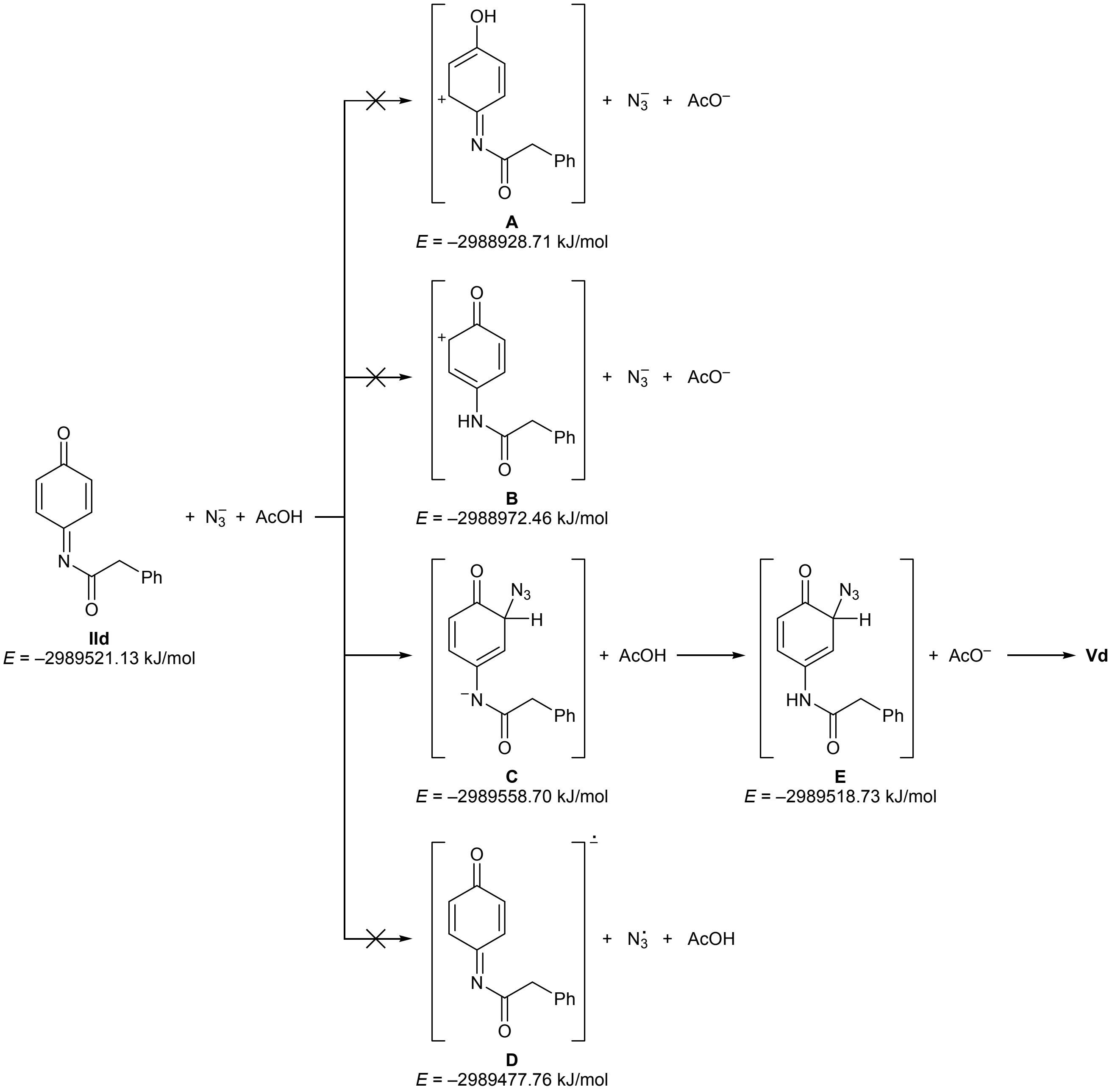
Compounds **IV**–**VI** remained unchanged on heating in boiling acetic acid, i.e., they did not undergo intramolecular redox transformation observed for azido derivatives of *N*-arylsulfonyl-1,4-benzoquinone imines [3]. Presumably, such behavior is determined by high redox potential of **IV**–**VI**, by analogy with *N*-aroyl- [2] and *N*-arylcarbamoyl derivatives [7].

Taking into account that the mechanism of reaction of *N*-substituted 1,4-benzoquinone imines was not studied previously, we analyzed possible reaction paths with the aid of quantum chemical calculations. Insofar as the reactions were carried out in acetic acid, first of all it was necessary to elucidate the structure of reacting nucleophile species. The pK_a value of hydrazoic acid is 4.59, which is close to pK_a of acetic acid (4.75) [8]; therefore, both azide ion and neutral hydrazoic acid molecule may be present in the system sodium azide–acetic acid. According to quantum chemical calculations, the equilibrium constant for the transformation $AcOH + N_3^- \rightleftharpoons HN_3 + AcO^-$ (calculated by the Gibbs equation [9]) is 5.2×10^{-6}, i.e., the reactive species is most likely to be azide ion.

Analysis of published data showed that the initial step in the reactions of quinone imines with nucleophile may be protonation of the substrate at the oxygen or nitrogen atom, addition of anionic nucleophile to neutral substrate molecule, and electron transfer with formation of quinone imine radical anion. In order to reveal which of the above reaction paths is most probable, we performed quantum chemical optimization of the corresponding intermediates **A**–**D** in the reaction with *N*-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetamide (**IId**) as model substrate (Scheme 2). As follows from the obtained data, the most probable initial step involves direct addition of azide ion to neutral molecule **IId** with formation of intermediate **C**, since the energy of the system comprising intermediate **C** and anions N_3^- and AcO^- is the lowest (Scheme 2; see figure). In the second step, proton addition to the nitrogen atom in **C** gives intermediate **E** whose aromatization finally yields 1,4-addition product **Vd**.

In summary, we have found that *N*-acyl-1,4-benzoquinone imines react with sodium azide via addition of azide ion to neutral quinone molecule, protona-

Scheme 2.



tion of quinone imine anion thus formed at the nitrogen atom, and subsequent aromatization to give 1,4-addition products.

EXPERIMENTAL

The ^{1}H NMR spectra were measured on a Varian VXR-300 instrument at 300 MHz using DMSO-d_6 as solvent and TMS as reference. The IR spectra were recorded on a UR-20 spectrometer from samples pelleted with KBr. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates; samples were applied from solutions in $CHCl_3$; plates were eluted with benzene–hexane (10 : 1), and spots were visualized under UV light.

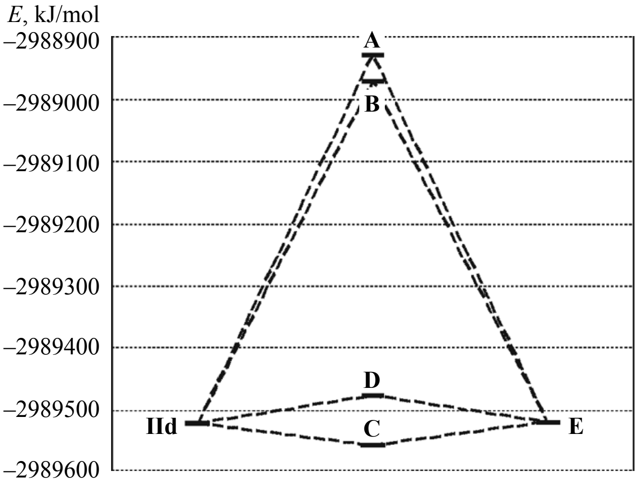
Quantum chemical calculations were performed with the aid of Firefly QC software package [10], which is based in part on the GAMESS (US) code [11]. The molecular structures were simulated in terms of the density functional theory using B3LYP functional and standard 6-31+G(*d*) basis set.

N-(4-Oxocyclohexa-2,5-dien-1-ylidene)-2-phenyl-(phenoxy, benzylidene)acetamides **Ia**–**Ic**, **IIa**–**IIc**, and **IIIa**–**IIIc** were prepared by oxidation of the corresponding *N*-(4-hydroxyphenyl) carboxamides with lead tetraacetate in acetic acid according to the procedure described in [6]; their physicochemical properties were consistent with those given in [6].

Reaction of quinone imines I–III with sodium azide (*general procedure*)**.** A solution of 4 mmol of sodium azide in a small amount of glacial acetic acid was added in one portion at room temperature to a solution of 2 mmol of quinone imine **Ia**–**Ic**, **IIa**–**IIc**, or **IIIa**–**IIIc** in 20 mL of glacial acetic acid. The solution turned red–brown and then (after 1–2 h) changed to light brown. If no solid separated from the reaction mixture, it was poured into a mixture of water with ice under vigorous stirring. The precipitate was filtered off, washed with water, dried, and recrystallized from benzene–hexane (1 : 2).

***N*-(5-Azido-4-hydroxy-2,3-dimethylphenyl)-3-phenylprop-2-enamide (IVa).** Yield 89%, mp 159–160°C. ^{1}H NMR spectrum, δ, ppm: 2.07 s (3H, 3-Me), 2.12 s (3H, 2-Me), 6.91 d (1H, CH=CH, J = 16.2 Hz), 7.06 s (1H, 6-H), 7.42–7.63 m (5H, Ph), 7.53 d (1H, CH=CH, J = 15.6 Hz), 8.88 br.s (1H, NH), 9.50 br.s (1H, OH). Found, %: N 18.78, 18.53. $C_{15}H_{12}N_4O_2$. Calculated, %: N 18.17.

***N*-(3-Azido-4-hydroxy-2,5-dimethylphenyl)-3-phenylprop-2-enamide (IVb).** Yield 92%, mp 219–220°C. ^{1}H NMR spectrum, δ, ppm: 2.03 s (3H, 5-Me), 2.17 s (3H, 2-Me), 6.90 d (1H, CH=CH, J = 15.9 Hz), 7.11 s (1H, 6-H), 7.39–7.63 m (5H, Ph), 7.53 d (1H, CH=CH, J = 15.9 Hz), 9.35 br.s (1H, NH), 9.52 br.s (1H, OH). Found, %: N 18.10, 18.51. $C_{17}H_{16}N_4O_2$. Calculated, %: N 18.17.



Energy diagram of the reaction of *N*-phenylacetyl-1,4-benzoquinone imine (**IId**) with sodium azide.

***N*-(3-Azido-4-hydroxy-2,6-dimethylphenyl)-3-phenylprop-2-enamide (IVc).** Yield 33%, mp 157–158°C. ^{1}H NMR spectrum, δ, ppm: 1.99 s (3H, 6-Me), 2.03 s (3H, 2-Me), 6.63 br.s (1H, 5-H), 6.85 d (1H, CH=CH, J = 15.9 Hz), 7.41–7.63 m (5H, Ph), 7.53 d (1H, CH=CH, J = 16.2 Hz), 9.34 br.s (1H, NH), 9.55 br.s (1H, OH). Found, %: N 18.03, 18.74. $C_{17}H_{16}N_4O_2$. Calculated, %: N 18.17.

***N*-(5-Azido-4-hydroxy-2,3-dimethylphenyl)-2-phenylacetamide (Va).** Yield 70%, mp 124–125°C. ^{1}H NMR spectrum, δ, ppm: 2.08 s (3H, 3-Me), 2.15 s (3H, 2-Me), 3.61 s (2H, CH_2), 6.83 s (1H, 6-H), 7.25–7.34 m (5H, Ph), 9.49 br.s (1H, NH), 9.51 br.s (1H, OH). Found, %: N 19.04, 19.47. $C_{14}H_{12}N_4O_2$. Calculated, %: N 18.91.

***N*-(3-Azido-4-hydroxy-2,5-dimethylphenyl)-2-phenylacetamide (Vb).** Yield 54%, mp 169–170°C. ^{1}H NMR spectrum, δ, ppm: 2.04 s (3H, 5-Me), 2.14 s (3H, 2-Me), 3.60 s (2H, CH_2), 7.01 s (1H, 6-H), 7.24–7.35 m (5H, Ph), 9.34 br.s (1H, NH), 9.51 br.s (1H, OH). Found, %: N 19.24, 19.78. $C_{16}H_{16}N_4O_2$. Calculated, %: N 18.91.

***N*-(3-Azido-4-hydroxy-2,6-dimethylphenyl)-2-phenylacetamide (Vc).** Yield 60%, mp 159–160°C. ^{1}H NMR spectrum, δ, ppm: 1.91 s (3H, 6-Me), 1.95 s (3H, 2-Me), 3.59 s (2H, CH_2), 6.57 s (1H, 5-H), 7.24–7.34 m (5H, Ph), 9.28 br.s (1H, NH), 9.45 br.s (1H, OH). Found, %: N 19.07, 19.62. $C_{16}H_{16}N_4O_2$. Calculated, %: N 18.91.

***N*-(5-Azido-4-hydroxy-2,3-dimethylphenyl)-2-phenoxyacetamide (VIa).** Yield 42%, mp 114–115°C. ^{1}H NMR spectrum, δ, ppm: 1.92 s (3H, 3-Me), 2.19 s (3H, 2-Me), 4.69 s (2H, OCH_2), 6.91 s (1H, 6-H), 6.98–7.34 m (5H, Ph), 9.53 br.s (1H, NH), 9.69 br.s (1H, OH). Found, %: N 18.59, 18.15. $C_{13}H_{10}N_4O_3$. Calculated, %: N 18.78.

***N*-(3-Azido-4-hydroxy-2,5-dimethylphenyl)-2-phenoxyacetamide (VIb).** Yield 75%, mp 163–164°C. ^{1}H NMR spectrum, δ, ppm: 1.99 s (3H, 5-Me), 2.17 s (3H, 2-Me), 4.66 s (2H, OCH_2), 6.89 s (1H, 6-H), 6.99–7.35 m (5H, Ph), 9.04 br.s (1H, NH), 9.29 br.s (1H, OH). Found, %: N 18.22, 17.97. $C_{15}H_{14}N_4O_3$. Calculated, %: N 18.78.

***N*-(3-Azido-4-hydroxy-2,6-dimethylphenyl)-2-phenoxyacetamide (VIc).** Yield 82%, mp 162–163°C. ^{1}H NMR spectrum, δ, ppm: 1.94 s (3H, 2-Me), 1.99 s (3H, 6-Me), 4.69 s (2H, OCH_2), 6.59 s (1H, 5-H), 6.95–7.34 m (5H, Ph), 9.18 br.s (1H, NH), 9.30 br.s (1H, OH). Found, %: N 18.35, 18.15. $C_{15}H_{14}N_4O_3$. Calculated, %: N 18.78.

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