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# Quantum-Chemical Substantiation of the Reactivity and Regioselectivity of Nitration of Biphenyl Derivatives

**E. R. Kofanov, A. V. Sokolov, A. V. Kolobov, and K. L. Ovchinnikov**

*Yaroslavl State Technical University, Yaroslavl, Russia*

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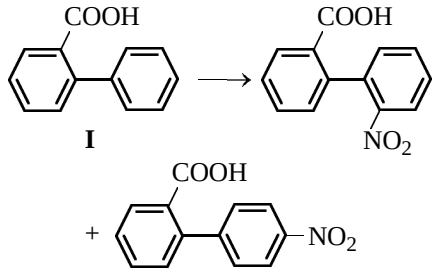
**Abstract** — Quantum-chemical calculations were used to substantiate the reactivity and regioselectivity of nitration of benzene, biphenyl, and carboxy-substituted biphenyls.

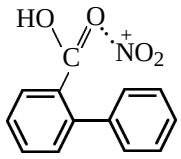
We earlier obtained experimental evidence showing that 2-biphenylcarboxylic acid (**I**) in $CH_3COOH$ is nitrated faster than benzene (**II**) and 3,4-biphenyldicarboxylic acid (**III**) but slower than biphenyl (**IV**) (Table 1).




**I**

The *ortho*-to-*para* nitration ratios for compound **I** in certain solvents attained 8.

To explain these facts, we proposed a model of the reaction, according to which the attacking species coordinates at the carboxy group of the substrate (structure **A**).




**A**

**Table 1.** Apparent partial rate constants of nitration of compounds **I**–**IV**

| Substrate | $k_o \times 10^4$, l mol$^{-1}$ s$^{-1}$ | $k_p \times 10^4$, l mol$^{-1}$ s$^{-1}$ |
|---|---|---|
| **I** | 5.8 | 3.4 |
| **II** | 2.5 | |
| **III** | 0.14 | 0.37 |
| **IV** | 13.0 | 24.0 |

To check and substantiate the proposed model, we performed quantum-chemical for nitration of benzene, biphenyl, and carboxy-substituted biphenyls. The calculations were peformed by the AM1 method in the gas-phase approximation [2]. As the model nitrating agent we chose the nitronium cation $NO_2^+$. The resulting potential energy surface profile is represented in Fig. 1.

It is known that the limiting stage of an SEAr reaction is σ-complex formation [3]. Therefore, it is this stage which we deal with in further discussion.

We performed direct calculations of transition states for the chosen objects. The heats of transition-state formation (activation barriers) fairly fit the experimental reactivities of the compounds (correlation coefficient 0.96, Fig. 2). Consequently, the calculation method used provides a noncontradictory explanation of the experimental results.

To explain the reactivity of the compounds in question, we attempted to find parameters descriptive of the reactivity. Relying on the linear-free energy principle, for such a reactivity index one can take reaction heat [heat of σ-complex formation ($\Delta N_\sigma$)] (Fig. 1).

Figure 3 represents the plot of the calculated activation energies vs. the heats of σ-complex formation.

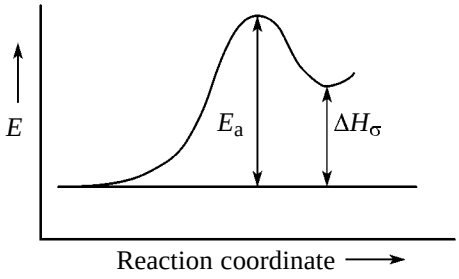



**Fig. 1.** Potential energy surface profile of an SEAr reaction.

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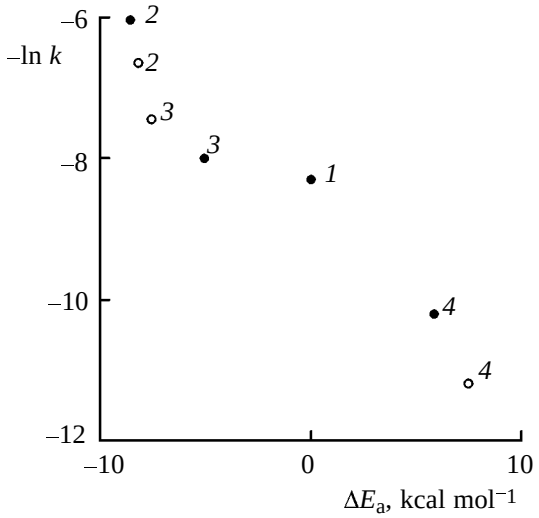


**Fig. 2.** Plot of the logarithm of the experimental partial nitration rate vs. activation barrier. (Dark circles) *para*-attack and (light circles) *ortho* attack (the activation barriers are related to that for benzene). (*1*) Benzene (**II**), (*2*) biphenyl (**IV**), (*3*) 2-biphenylcarboxylic acid (**I**), and (*4*) 3,4-biphenyldicarboxylic acid (**III**).

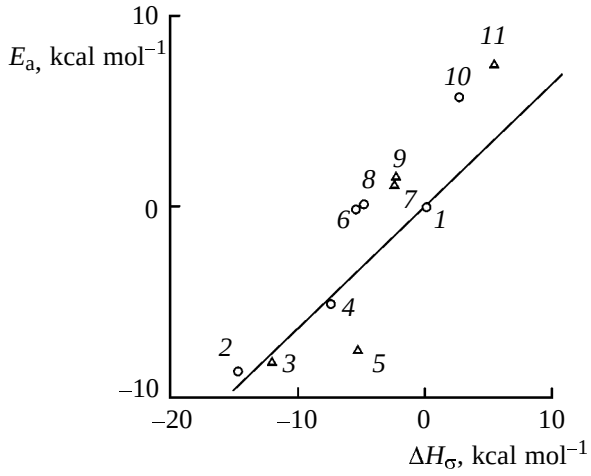


**Fig. 3.** Plot of activation energy vs. heat of σ-complex formation (relative to benzene). (*1*) Benzene, (*2, 3*) biphenyl, (*4, 5*) 2-biphenylcarboxylic acid (**I**), (*6, 7*) 3-biphenylcarboxylic acid (**V**), (*8, 9*) 4-biphenylcarboxylic acid (**VI**), and (*10, 11*) 3,4-biphenyldicarboxylic acid (**III**) [(circles) *para* attack and (triangles) *ortho*-attack].

There is a correlation dependence between these values, but the points are considerably scattered, implying that the behavior of the corresponding compound fails to fit the linear free-energy principle. The deviations may result from the influence of a certain factor (specific interaction), which shows up either in the saddle point or in the σ-complex region (i.e. affects $E_a$ or on $\Delta N_\sigma$). We suggest that this factor is Coulomb interaction. In the transition state the charge on the attacking species is still preserved (Table 2), while in the σ complex the positive charge is fully delocalized on the benzene ring, and the residual charge on the nitro group is ca. 0.01–0.02 *e*; therefore, in the latter case the Coulomb interaction between $NO_2^+$ and the carboxy group can be neglected. For the baseline in the plot (Fig. 3) we chose the line that joins the points for unsubstituted benzene and biphenyl. The points lying above the baseline relate to Coulomb repulsion between the substituent in the substrate and the attacking species and those lying below the baseline, to attraction. Table 2 lists the calculated energies of the Coulomb repulsion between $NO_2^+$ and the substituent (COOH) in the second benzene ring. The calculations were performed using a procedure for energy separation, that allows estimation of the energy of interaction of chemically nonbonded groups.

**Table 2.** Contribution of the energy of $NO_2^+$–COOH interaction into the total energy of the transition state (by the results of energy separation)[a]

| Parameter | **I** | **V** | **VI** | **III** |
|---|---|---|---|---|
| | | *ortho* Attack | | |
| $E_{tot}$, eV | –0.245 | 0.091 | 0.074 | 0.188 |
| $E_{Coul}$, eV | –0.238 | 0.091 | 0.075 | 0.190 |
| $Q_{COOH}$, *e* | 0.002 | 0.043 | 0.047 | 0.072, 0.045 |
| $Q_{NO_2}$, *e* | 0.399 | 0.375 | 0.381 | 0.395 |
| $Q_N$, *e* | 0.619 | 0.579 | 0.581 | 0.591 |
| | | *para* Attack | | |
| $E_{Coul}$, eV | –0.159 | 0.065 | 0.050 | 0.130 |
| $Q_{COOH}$, *e* | 0.003 | 0.038 | 0.042 | 0.070, 0.041 |
| $Q_{NO_2}$, *e* | 0.398 | 0.411 | 0.414 | 0.422 |
| $Q_N$, *e* | 0.591 | 0.581 | 0.583 | 0.592 |

[a] ($E_{tot}$) Total energy, ($E_{Coul}$) Coulomb contribution, and (*Q*) charge.

This interaction is a charge–dipole interaction and, consequently, the strength of the interaction is much dependent on the orientation of the carboxy group. The carboxy group is almost neutral, the atomic charges are +0.3 (C), –0.3, –0.3 (O), and +0.2 (H), the positive charge of the attacking nitronium cation is localized on the nitrogen atom, and it is still high in the transition state (Table 2, Fig. 4).

Table 2 and Fig. 4 show that the reaction with 2-biphenylcarboxylic acid (**I**) is the only that may

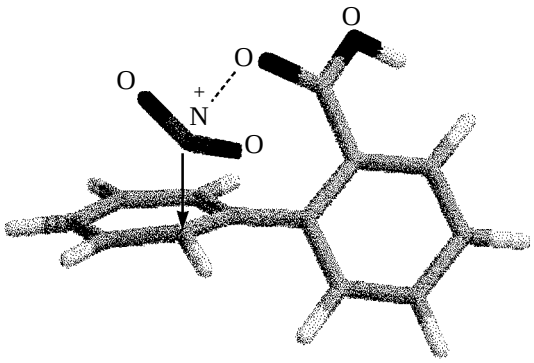


**Fig. 4.** Structure of the transition state for nitration of 2-biphenylcarboxylic acid (**I**) (*ortho* attack).

occur with energy reduction occur. In the case of the *ortho* attack, when the carboxy group is turned by the negatively charged oxygen atoms to the nitronium cation and the distance between the reacting species is smaller than in the case of the *para* attack, this effect is the strongest ($E_{tot}$ –0.245 eV). As a result, the relative reactivity of compound **I** is enhanced (Table 1). This model also explains the anomalously high *ortho*/*para* mononitration ratio with 2-biphenylcarboxylic acid.

With the other substrates, the $E_{tot}$ value is positive, and the corresponding points lie above the baseline. Thus, the fact that the behavior of the substrates fails to fit the linear free-energy principle is explained by additional (compared with σ complex) Coulomb interaction in the transition state (Fig. 3).

## EXPERIMENTAL

Nitration was performed at a 1 : 47 : 115 substrate : $HNO_3$ : $CH_3COOH$ molar ratio at 70°C. Analysis of methyl biphenylcarboxylates and nitration products was performed on a Chrom-5 chromatograph with a flame-ionization detector on a 1500 × 3-mm column packed with 5% SE-30 on Chromaton N-AW. Injector temperature 260°C. Oven temperature 200 (acid **I**) and 230°C (acid **III**). Carrier gas nitrogen, flow rate $6.3 \times 10^{-7}$ $m^3/s$. Analysis of biphenyl and its nitration products was performed on an LKhM-80 chromatograph with a flame-ionization detector on a 2500 × 3-mm column packed with 10% SKTF-50kh on Chromaton N-AW-DMCS. Injector temperature 260°C. Oven temperature 204°C. Carrier gas helium, flow rate $5 \times 10^{-7}$ $m^3/s$.

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