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The MNDO-PM3 study of the mechanism of nucleophilic substitution of the phenoxide anion for the nitro group in 1,3,5-trinitrobenzene and 2,4,6-trinitrotoluene in the gas phase and in polar solvents

*V. N. Solkan** *and S. A. Shevelev*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 117913 Moscow, Russian Federation.
Fax: +7 (095) 135 5328

The semi-empirical quantum chemical MNDO-PM3 calculations of the enthalpies of formation of Meisenheimer *ortho*- and *ipso*-σ-complexes of 1,3,5-trinitrobenzene (TNB) and 2,4,6-trinitrotoluene (TNT) with the phenoxide anion in the gas phase and in water are performed within the framework of the point dipole model. Based on the calculated heats and activation barriers to substitution of the nitro group by the phenoxyl group in TNB and TNT, the possibility of the reactions of TNB and TNT with the phenoxide anion in water is shown. These reactions in water occur *via* the S_NAr mechanism involving the corresponding *ipso*-σ-complex as an intermediate. In the gas phase, the S_NAr mechanism is impossible, because the reaction is strongly endothermic. In the case of TNT, the exothermic reaction of elimination of a proton from the methyl group by the phenoxide anion competes with nucleophilic substitution in a polar solvent. The activation energy calculated for this exothermic reaction is 8 kcal mol^{-1}.

Key words: Meisenheimer complexes; 1,3,5-trinitrobenzene; 2,4,6-trinitrotoluene; MNDO-PM3 method; reaction mechanism; solvation; proton transfer.

This work continues the series of theoretical studies of the possibility of the nucleophilic substitution of an aromatic nitro group not activated by *ortho*- and *para*-substituents. Polynitrobenzenes and their derivatives with nitro groups at *meta*-positions were chosen for the study. First of all, these are 1,3,5-trinitrobenzene (TNB) and 2,4,6-trinitrotoluene (TNT), for which *ipso*-substitution of the nitro group is not the most typical result of the reaction with nucleophiles. Rather, the reaction with nucleophiles leads to the formation of strong σ-complexes due to the addition of the nucleophile to the carbon atom of the cycle at the *ortho*-position to the nitro group, *i.e.*, *ortho*-σ-complexes (Meisenheimer *ortho*-complexes, *o*-MC).[1,2] The elimination of a proton from the methyl group through the action of the base nucleophile is also characteristic of TNT.[1,2]

The possibility of the reaction of the methoxide ion with TNB or TNT *via* the S_NAr mechanism to form the corresponding *ipso*-σ-complex as an intermediate has been previously studied[3] by the MNDO-PM3 method,[4] taking into account the solvent effect in terms of the pseudo-continuous model of point dipoles (PD).[5,6] Based on the calculated enthalpies of the formation of the *ipso*- and *ortho*-σ-complexes TNB · $^{-}$OMe and TNT · $^{-}$OMe and the heats of their decomposition with elimination of NO_2^- or H^-, respectively, the conclusion has been made that substitution of the nitro group of TNB is possible in a strong polar solvent *via* the S_NAr mechanism, despite the competitive process of *o*-MC formation. It is shown that the formation of the trinitrobenzyl anion is the most probable for the reaction of $^{-}$OMe with TNT.

However, when the cross section of the potential energy surface (PES) was calculated along the reaction coordinate of addition to TNB and TNT to form the *ortho*- and *ipso*-σ-complexes, the corresponding activation barriers were not estimated, because contact between the reagents resulted not in the addition of $^{-}$OMe, but in the transfer of an electron from the methoxide ion to the benzene ring. A special report will be devoted to the consideration of the one-electron transfer mechanism for the nucleophilic substitution of the non-activated nitro group. In this work, the reactions of TNB and TNT with the phenoxide ion, which is characterized by a higher ionization potential[7] and a lower basicity[8] than the methoxide ion, are studied by the MNDO-PM3 method, taking into account the effects of a polar solvent in terms of the PD model.

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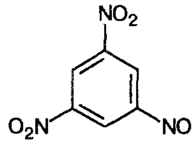
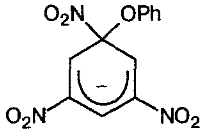
Table 1. Enthalpies of formation of compounds in the gas phase and in an aqueous solution calculated by the MNDO-PM3 method

Compound	$\Delta_f H$(gas) /kcal mol^{-1}	$\Delta_f H$(solv.) /kcal mol^{-1}
TNB*	6.9	–
1	−55.9	−97.5
2	−84.5	−126.7
3	8.9	–
4	15.9	–
TNT*	3.3	–
5	−51.1	−93.2
6	−53.3	−95.7
7	−77.1	−119.7
8	9.2	–
9	6.9	–
10	17.7	–
11*	−59.7	−100.5
$C_6H_5O^-$	−44.1	−104.2
NO_2^-*	−42.9	−121.9

* See Ref. 3.



TNB



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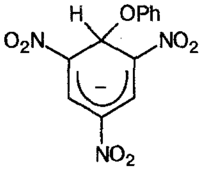

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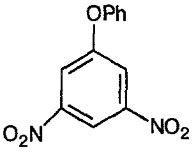

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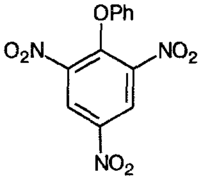

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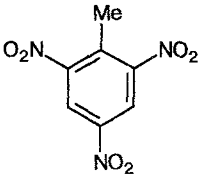

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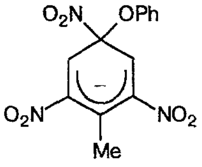

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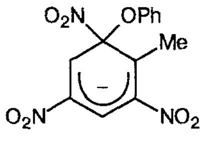

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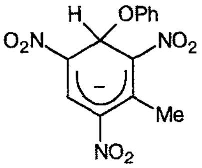

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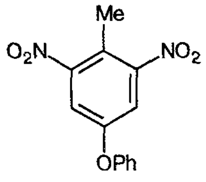

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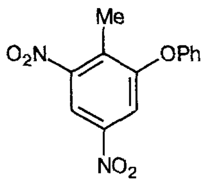

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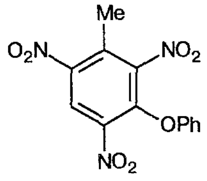

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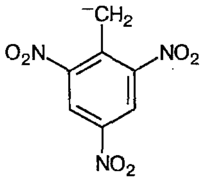

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Calculation Procedure

The quantum chemical calculations were performed by the MORAS program developed on the basis of the MOPAC program complex (version 3.10)[9] with the purpose of realizing the MNDO-PM3 method[4] and the pseudo-continuous PD model.[6] The routes of the addition of the phenoxide ion to TNB and TNT to form *ortho*- and *ipso*-σ-complexes TNB · $^-$OPh and TNT · $^-$OPh (Table 1) and of the elimination of the nitrite ion from the *ipso*-σ-complexes were minimized in energy and determined by the reaction coordinate procedure (RC).[10,11]. In the case of the addition of $^-$OPh to TNB and TNT, the distances *R*(C(H)...$^-$OPh) and *R*(C(NO_2)...$^-$OPh) calculated from the equilibrium bond length C—OPh in the *ortho*- and *ipso*-σ-complexes, respectively, were taken as RC. For the elimination of the nitrite ion from the *ipso*-σ-complexes TNB · $^-$OPh and TNT · $^-$OPh, the distance calculated from the equilibrium bond length C—NO_2 was taken as the RC.

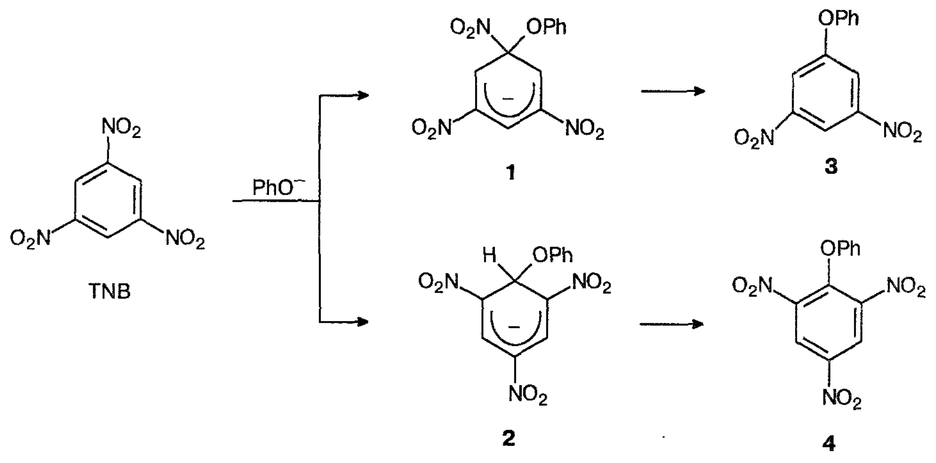
The types of stationary points on the PES were established by calculating the eigenvalues of the force constant matrix.[12] The parameters of the PD model used in the consideration of effect of a polar solvent on the reaction energetics were assumed to be equal to those of water.[6] All calculations were performed on an ES 1066 computer.

Results and Discussion

As has been previously mentioned,[3] to determine the possibility of nucleophilic substitution *via* the S_NAr mechanism (see Ref. 13), it is necessary to calculate the enthalpies of formation $\Delta_f H$ for the reagents, products, MC, and the two transition states corresponding to the formation and decomposition of the *ipso*-MC, respectively. The most important task is the estimation of the stability of the *ipso*-MC, due to special symmetric position of the latter in the S_NAr reaction coordinate. It has been previously shown[3] that $\Delta_f H$ of an *ipso*-MC can be considered as an index of its reactivity.

In this work, $\Delta_f H$ for all isomeric MC, TNB · $^-$OPh and TNT · $^-$OPh, and the corresponding products of the substitution reaction and the reaction with the phenoxide ion (Scheme 1, see Table 1) are calculated by the MNDO-PM3 method with the complete optimization of geometry. Based on the $\Delta_f H$ values obtained and calculated previously,[3] the enthalpies $\Delta_r H$(gas) of the

Scheme 1



formation of MC and products of the substitution of a phenoxyl group for the nitro group in the gas phase are determined (Table 2). To take into account the effect of a strong polar solvent on the thermodynamic parameters of the reactions studied, the solvation energies of the anions in an aqueous solution $\Delta_f H$(solv.) are calculated by the MNDO-PM3-PD procedure (see Table 1).

The values of $\Delta_f H$(solv.) obtained make it possible to estimate the effect of a strong polar solvent (H_2O) on the $\Delta_r H$ values (Table 2). It should be mentioned that the calculated values of $\Delta_f H$(gas) are used for the calculation of $\Delta_r H$(solv.) for neutral molecules, because the energy of non-specific solvation of uncharged species usually does not exceed 5 to 7 kcal mol^{-1}, and the PD procedure does not allow one to estimate such small values with satisfactory accuracy. It is important to emphasize that the error related to neglecting the solvation energy of neutral molecules in the estimation of $\Delta_r H$(solv.) decreases considerably due to the partial compensation of the corresponding contributions for neutral molecules in the left and right parts of the chemical equations presented in Table 2.

Table 2. Enthalpies of reactions in the gas phase and in an aqueous solution calculated by the MNDO-PM3 method

Reaction		$\Delta_r H$(gas)	$\Delta_r H$(solv.)
		/kcal mol^{-1}	
TNB + $^-$OPh → **1**	(1)	−18.7	−0.2
TNB + $^-$OPh → **2**	(2)	−47.3	−29.4
1 → **3** + NO^-_2	(3)	21.9	−15.5
TNB + $^-$OPh → **3** + NO^-_2	(4)	3.2	−15.7
TNT + $^-$OPh → **5**	(5)	−10.3	7.7
TNT + $^-$OPh → **6**	(6)	−12.5	5.2
TNT + $^-$OPh → **7**	(7)	−36.3	−18.8
5 → **8** + NO_2^-	(8)	17.4	−19.5
6 → **9** + NO_2^-	(9)	17.1	−19.5
TNT + $^-$OPh → **8** + NO_2^-	(10)	7.1	−11.8
TNT + $^-$OPh → **9** + NO_2^-	(11)	4.6	−14.3
TNT + $^-$OPh → **11** + PhOH	(12)	−40.5	−21.2
2 → **4** + H^-	(13)	134.0	—
7 → **10** + H^-	(14)	128.4	—

As can be seen from Table 2, the addition of the phenoxide ion to TNB in the gas phase is exothermic (reactions (1) and (2), $\Delta_r H$(gas)), but to a smaller extent than for $^-$OMe. Moreover, the calculated values of $\Delta_r H$(gas) indicate rather high stabilities of the *ortho*- and *ipso*-σ-complexes in the gas phase (see Table 2). In fact, the calculated heat of the elimination of the nitrite ion from the *ipso*-σ-complex TNB • $^-$OPh in the gas phase testifies that this process is thermodynamically unfavorable (reaction (3), $\Delta_r H$(gas)). The elimination of the hydride ion from the corresponding *ortho*-σ-complex (reaction (13)) is less favorable. The calculated data obtained suggest that the substitution of the nitro group of TNB by a phenoxyl group is impossible in the gas phase *via* the two-stage S_NAr mechanism, which includes the addition of the nucleophile and subsequent elimination of the nitrite ion from the *ipso*-σ-complex.

Taking into account the ionic character of the reaction studied, it would be expected that the solvent polarity would have a strong effect on its thermodynamic parameters. In fact, the estimate of the enthalpy of reaction (3) in a strong polar solvent ($\Delta_r H$(solv.)) presented in Table 2 indicates a noticeable change in the energy of the elimination of the nitrite ion from the *ipso*-σ-complex TNB • $^-$OPh: the reaction becomes exothermic. However, unlike the formation of the *ipso*-σ-complex TNB • $^-$OMe (see Ref. 3), the formation of the *ipso*-σ-complex TNB • $^-$OPh in a strong polar solvent is almost thermally neutral (see Table 2).

The position of the *ipso*-σ-complex TNB • $^-$OPh on the PES predicted by the MNDO-PM3-PD method is in agreement with the available data on the fact that the reactions of MC formation in solution are approximately thermally neutral.[1] The cross section of the PES of the combined molecular system TNB+$^{-}$OPh along the RC *R*(C(NO$_2$)...$^{-}$OPh) calculated by MNDO-PM3-PD indicates a comparatively low activation barrier (12 kcal mol^{-1}) to *ipso*-MC formation. For the exothermic reaction of *ortho*-MC formation, the calculated cross section of the PES along the RC *R*(C(H)...$^{-}$OPh) gives a lower (2.5 kcal mol^{-1}) activation barrier in a strong polar solvent than for *ipso*-MC formation. However, if it is taken into account that all known semi-empirical quantum chemical methods based on the MNDO Hamiltonian (MNDO, AM1, and PM3) overestimate[13,14] the stability of *ortho*-MC, it can be assumed that the value of $\Delta_r H$ calculated by MNDO-PM3 for the formation of the *ortho*-MC TNB $\cdot$ $^{-}$OPh in the liquid phase is also decreased. Owing to this, the activation barrier is also decreased.

The introduction of the correction for $\Delta_r H$ of *ortho*-MC formation makes it possible to refine the value of the activation energy E_a, according to the Bell—Evans—Polany (BEP) correlation $\delta(E_a) = k \cdot \delta(\Delta_r H)$. It is evident that in the case of the *ortho*-MC (TNB $\cdot$ $^{-}$OPh), the correction for $\Delta_r H$ should ensure that the reaction of its formation is approximately thermally neutral in character, *i.e.*, the correction for $\Delta_r H$ can be 25 to 30 kcal mol^{-1} in the case of a strong polar solvent. Then, according to the BEP correlation, the correction to the calculated value of E_a cannot exceed 25 to 30 kcal mol^{-1}. It is easy to notice that this correction to the activation barrier (even at $k = 0.5$) for the formation of *ortho*-MC TNB $\cdot$ $^{-}$OPh ensures that the correlation $E_a(2) \geq E_a(1)$ is fulfilled and hence, allows one to describe the first stage of the nucleophilic substitution of the nitro group of TNB by a phenoxyl group in terms of the traditional scheme of an S$_N$Ar reaction:

$$\textit{ortho}\text{-}\sigma\text{-complex TNB} \cdot {}^{-}\text{OPh} \rightleftharpoons$$

$$\rightleftharpoons \text{TNB} + {}^{-}\text{OPh} \rightleftharpoons \textit{ipso}\text{-}\sigma\text{-complex TNB} \cdot {}^{-}\text{OPh}.$$

For the second stage of nucleophilic substitution, the elimination of the nitrite ion from the *ipso*-σ-complex, the activation energy found by the MNDO-PM3-PD method is 5.5 kcal mol^{-1} in a strong polar solvent. Thus, according to the MNDO-PM3-PD method, the transformation of the *ipso*-complex TNB $\cdot$ $^{-}$OPh into 1-phenoxy-3,5-dinitrobenzene *via* the S$_N$Ar mechanism is possible only in a strong polar solvent. It should be especially emphasized that the noticeable destabilization of the *ipso*-σ-complex TNB $\cdot$ $^{-}$OPh as the solvent polarity increases allows one to hope that the conditions of this nucleophilic substitution of a phenoxyl group for a nitro group can be optimized by selecting a solvent of the necessary polarity. The *ortho*-MC is the most probable product of the reaction of TNB with the phenoxide ion, because it is the most thermodynamically favorable.

Let us consider the results of the calculations of the reaction of the phenoxide ion with TNT. The calculated values of $\Delta_f H$ for the σ-complexes TNT $\cdot$ $^{-}$OPh and the corresponding products are presented in Table 1. The enthalpies of the reactions, $\Delta_r H$, presented in Table 2 are determined on the basis of these values of $\Delta_f H$. The analysis of the data in Table 2 shows that the addition of the phenoxide ion to TNT (reactions (5)—(7)) in the gas phase is characterized by a substantial exothermic effect. The calculated values of $\Delta_r H$(gas) for reactions (8) and (9) in the gas phase indicate that these routes of the decomposition of the *ipso*-σ-complexes TNT $\cdot$ $^{-}$OPh are to a large extent endothermic. The elimination of the hydride ion from *ortho*-σ-complex **7** in the gas phase (reaction (14)) is more endothermic. Therefore, the replacement of the nitro group in TNT in the reaction with the phenoxide ion in the gas phase cannot occur *via* the stages of addition—elimination according to the S$_N$Ar mechanism. It should be emphasized that overall reactions (10) and (11) are also endothermic.

As can be seen from Table 2, a strong polar solvent dramatically changes the values of $\Delta_r H$ for reactions (8) and (9): the elimination of the nitrite anion from the anionic *ipso*-σ-complexes becomes strongly exothermic. Overall reactions (10) and (11) also turn out to be noticeably exothermic. The cross sections of the PES for reactions (8) and (9) were calculated by the MNDO-PM3 method, using the C—NO$_2$ distance as the RC and optimizing all remaining geometric parameters of the *ipso*-σ-complexes (TNT $\cdot$ $^{-}$OPh) for each point along the RC. The energy profiles obtained testify that the elimination of NO$_2^-$ in a strong polar solvent occurs with the low barriers: 3.4 and 3.8 kcal mol^{-1}, respectively.

Thus, according to the calculations, the reaction of TNT with the phenoxide ion can occur *via* the S$_N$Ar mechanism only in a strong polar solvent. It is noteworthy that the transition to the solvent with the maximum polarity (H$_2$O, $\varepsilon = 80$) results in the significant destabilization of the *ipso*-σ-complexes TNT $\cdot$ $^{-}$OPh (reactions (5) and (6), see Table 2). Owing to this, the reactions of the elimination of the nitrite ion from the *ipso*-σ-complexes mentioned become strongly exothermic. It is evident that the use of a medium polar solvent ($\varepsilon = 20$ to 40) results, on the one hand, in a smaller destabilization of the *ipso*-σ-complexes TNT $\cdot$ $^{-}$OPh and, on the other hand, in fairly exothermic elimination of the nitrite anion.

Taking into account the low activation barriers for these reactions of the elimination of the nitrite anion, it can be assumed that even a twofold decrease in the heats of reactions (5) and (6) in a medium polar solvent does not result in a critical increase in their activation energies. It also follows from the calculations by the MNDO-PM3 method that the reaction of TNT with the phenoxide ion in the gas phase can be accompanied by exothermic deprotonation to form the trinitrobenzyl anion: $\Delta_r H$(gas) $= -40.5$ kcal mol^{-1} (see Table 2, reaction

(12)). The calculation of this reaction in the strong polar solvent also results in negative enthalpy: $\Delta_r H$(solv.) = −21.2 kcal mol^{-1}.

To estimate the barrier of the transfer of a proton from the methyl group of TNT to the $^-$OPh anion, the energy profile for reaction (12) was calculated, using the C(sp^3)—H distance as the RC and optimizing all remaining geometric parameters of the complex with the hydrogen bond (2,4,6-$(NO_2)_3$—C_6H_2Me...$^-$OPh) for each point along the RC. The energy profile obtained testifies that the proton transfer occurs with a low activation barrier of ~8 kcal mol^{-1}. It is of interest that the calculation of the complex with the H bond (2,4,6-$(NO_2)_3$—C_6H_2Me...$^-$OMe) by the MNDO-PM3-PD method indicates that the transfer of a proton from the methyl group of TNT to the oxygen atom of the $^-$OMe anion occurs without a barrier. One can expect on the basis of the data obtained that the introduction of less basic nucleophiles than $^-$OPh into the reaction with TNT would make it possible to significantly retard the process of the elimination of a proton from the methyl group of TNT and to direct the reaction mainly *via* the S$_N$Ar mechanism of nucleophilic substitution.

Summarizing the results obtained, let us emphasize that despite the competitive process of the formation of stable *ortho*-MC, substitution of the nitro groups in TNB and TNT *via* the S$_N$Ar mechanism is possible in solvents of strong and medium polarities.

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