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Change in regioselectivity in the monoreduction of 2,4,6-trinitrotoluene with titanium(III) and vanadium(II) ions in the presence of iron(II) and copper(II) salts*

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Small additives of iron(II) or copper(II) salts change the regioselectivity of 2,4,6-trinitrotoluene monoreduction with titanium(III) chloride affording predominantly less accessible 2-amino-4,6-dinitrotoluene over 4-amino-2,6-dinitrotoluene (from 25% when the reduction occurs in the absence of the iron and copper salts to 70% in the presence of these salts). A possible mechanism of the process is discussed.

Key words: 2,4,6-trinitrotoluene, monoreduction, 2-amino-4,6-dinitrotoluene, 4-amino-2,6-dinitrotoluene. regioselectivity, titanium(III), vanadium(II), iron(II), copper(II).

2-Amino-2,6-dinitrotoluene (**1**) and 4-amino-4,6-dinitrotoluene (**2**) are the promising substrates for organic synthesis due to the simultaneous presence of the amino and nitro groups. Therefore, it is necessary to develop selective methods of their synthesis, one of which is the regioselective reduction of 2,4,6-trinitrotoluene (TNT).[1] This problem is also of interest from the viewpoint of a principal problem in organic chemistry: to elucidate factors affecting the regioselectivity of partial reduction of aromatic polynitro compounds (PNC).

In our previous study, we described[2] the direct electrochemical monoreduction of TNT to form isomeric dinitro(hydroxyamino) derivatives and considered the mechanism and factors that result, possibly, in similar regioselectivity of the electroreduction and monoreduction by trivalent titanium and bivalent vanadium ions.

In the earlier works on studying of effect of different factors on the regioselectivity (except for the works[3,4] where the authors attempted to explain the role of components of the medium in determination of the direction of reduction of some aromatic PNC), the reducing agents, which are reactive toward the *para*- or *ortho*-nitro groups, were usually selected[5] for the preparation of some aromatic nitroamines. For instance, the tin(II) salts reduce more actively the *o*-nitro groups of TNT[6] and, on the contrary, the titanium(III) salts are more active in the reduction of the *p*-nitro group.[7] In the catalytic hydrogenation of aromatic PNC in the presence of iron powder, as in the case of tin(II), the monoreduction of the *o*-nitro groups proceeds more easily.[8]

We have previously[9,10] found that the reduction of aromatic mono- and polynitro compounds, including TNT, by the titanium(III) salts, is accelerated in the presence of bivalent iron and bivalent copper ions, for example, by 2 and 8 times in the presence of $FeSO_4$ in concentrations of 0.01 and 0.3 mol L^{-1}, respectively. In this case, the concentration of the titanium(III) salts was 1 mol L^{-1}. The introduction of nickel, chromium, vanadium, and alkaline-earth metal cations into the reaction mixture has no noticeable effect on the reduction rate of TNT by the titanium(III) ions. Thus, the influence of the iron(II) and copper(II) ions on this process is specific.

When assuming that the catalytic effect of the iron(II) and copper(II) ions on PNC reduction is caused by the formation of complexes of these ions with the starting compound or its radical anions (RA) generated after an electron was transferred to the substrate, then one can expect a change in the regioselectivity of the process in the presence of these ions. This assumption is based on published data,[3,4,7,11] which show that the regioselectivity of PNC reduction is caused by the charge and unpaired electron density distribution in the RA. This distribution determines the predominant direction of protonation and, as a consequence, formation of a particular isomer by partial reduction. A similar approach was used in the quantum chemical study of the regioselectivity of aromatic PNC reduction.[12] The formation of an RA complex with metal ions can change significantly the electron density distribution and direction of RA protonation. To check this assumption, we carried out experiments on the partial

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reduction of TNT by titanium(III) ions in the presence of iron(II) and copper(II) ions.

Experimental

Reduction of TNT was carried out using an aqueous acidic (HCl concentration 6—8%) solution of $TiCl_3$. This solution was prepared by the electrochemical reduction of $TiCl_4$ (special-purity grade) conducted in the galvanostatic mode on a lead electrode with a current of 1.0 A (platinum served as an anode, and the anolyte was 7% H_2SO_4). The Ti^{3+}/Ti^{4+} ratio was polarographically monitored during electrolysis. The concentration of Ti^{3+} ions was determined by titration with a standard solution of potassium bichromate using diphenylamine as the indicator.

Partial reduction of TNT in the absence of iron or copper salts. A solution of TNT (1 g) in MeOH (100 mL) was rapidly mixed with an aqueous solution of a reagent (10 mL) containing $TiCl_3$ (0.7—1.6 mol L^{-1}) and HCl (1.5—2.0 mol L^{-1}). The acidity of the medium was provided by the addition of concentrated HCl (6 mL) to a methanolic solution of the substrate. Several minutes after mixing, the reaction soup gained a bright yellow color. Methanol was removed under reduced pressure, water (50 mL) was added, and extraction with $CHCl_3$ (3×30 mL) was performed. Then, the aqueous layer was treated with concentrated NH_4OH to achieve pH 8—9 and again extracted with $CHCl_3$. The chloroform extracts were combined, washed with water, and concentrated. In some cases, the extracts from acidic and alkaline media were studied separately.

Monoreduction of TNT by vanadium(II) was carried out similarly.

Partial reduction of TNT in the presence of iron or copper salts. Salt $FeSO_4$ (0.008—0.016 mol L^{-1}) or $CuCl_2$ (0.003—0.0245 mol L^{-1}) was added to a solution of $TiCl_3$, and further the reaction was carried out according to the above-described procedure. 2-Amino-4,6-dinitrotoluene (**1**) and 4-amino-2,6-dinitrotoluene (**2**) were synthesized in an overall yield of 85—95% with respect to the reacted TNT.

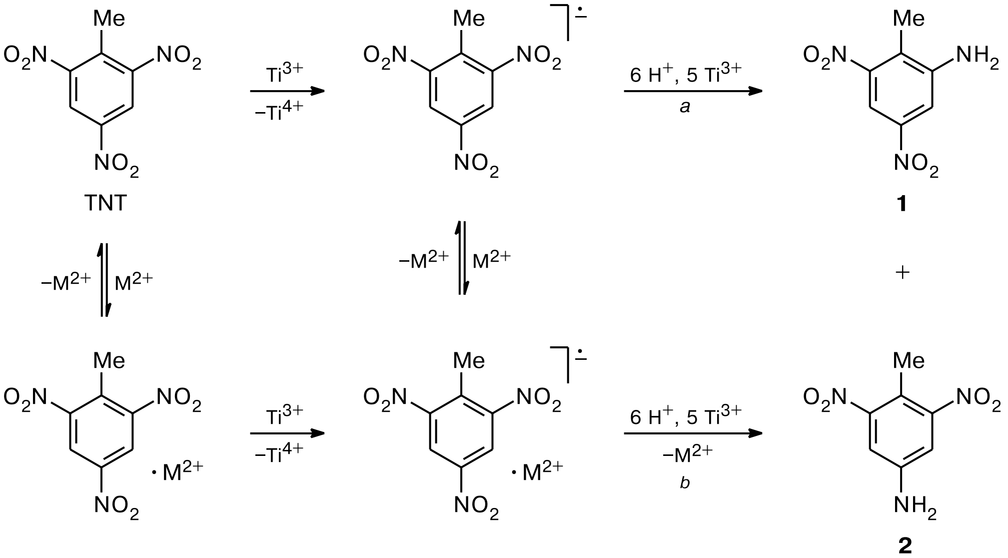
The prepared mixtures of products were analyzed by ^1H NMR spectroscopy and TLC on Sorbfil plates with the UV indicator in a hexane—ether (1 : 4) system. ^1H NMR spectra were recorded in $(CD_3)_2CO$ on a Bruker AC-200 spectrometer. The spectrum of compound **1** exhibits a characteristic singlet at δ 7.78. That of compound **2** has a characteristic singlet at δ 7.35. The content of each component in a mixture was determined from integral intensities of the corresponding signals of 1,3,5-trinitrobenzene used as an internal standard.

Results and Discussion

Iron(II) ions in a concentration of 0.001 mol L^{-1} and higher change substantially the regioselectivity of TNT monoreduction by the titanium(III) ions toward the predominant formation of the 2-amino derivative (Scheme 1). The content of isomer **1** in a mixture of products after reduction increases from 25 to 50% at a concentration of $FeSO_4$ of 0.0023 mol L^{-1}. For the further increase in $FeSO_4$, the fraction of **1** reaches a limiting value equal to 60% (Fig. 1, curve *1*). A similar but lower effect was detected in the case of TNT monoreduction with vanadium(II) in the presence of iron(II) ions (see Fig. 1, curve *2*).

The change in regioselectivity observed is not due to the effect of the iron salt as a reducing agent, because the Fe^{3+}/Fe^{2+} system has a much higher redox potential (+0.77 V) than the Ti^{4+}/Ti^{3+} pair (–0.04 V). In control entries, the TNT conversion in the presence of excess $FeSO_4$ is only 10% within a week, while with the titanium(III) ions the reaction completes for 20 s.

Scheme 1



a. **1** : **2** = 1 : 3; *b*. **1** : **2** = 2 : 1 (for M = Fe)

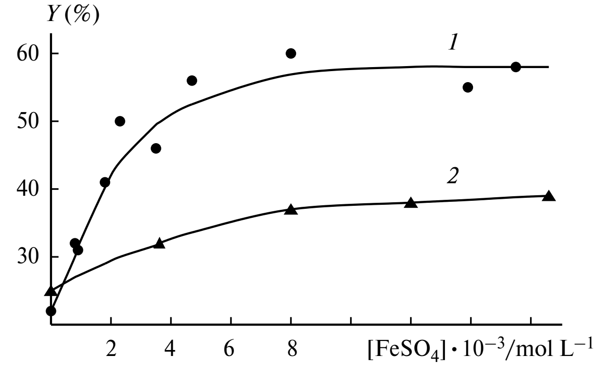


Fig. 1. Relative content of 2-amino-4,6-dinitrotoluene (**1**) (Y) in mixture **1**—**2** for partial TNT reduction (C = 0.04 mol L^{-1}) by $TiCl_3$ (*1*) and VCl_2 (*2*) *vs.* $FeSO_4$ concentration in the reaction mixture (85 vol.% MeOH) containing 3% HCl (concentrations of $TiCl_3$ and VCl_2 0.1 and 0.07 mol L^{-1}, respectively; TNT conversion 30—50%; 20—25 °C).

The use of $TiCl_3$ together with iron salts for a quantitative analysis of some nitramines (nitroguanidine, cyclotrimethylenetrinitramine) and for the stoichiometric reduction of organic derivatives of nitric acid is indicated in literature.[13—16] A reason for the positive influence of the iron(II) ions on the extent of reduction is considered only in one work.[15] Iron(II) ions were suggested[15] to interact with hydrolytically unstable (hydroxyamino)guanidine formed intermediately from nitroguanidine to produce a more stable complex ion, which is further reduced with the titanium(III) ions. A high excess of the iron salt is used in the analysis and, most likely, the function of the iron ions in the reduction process is not catalytic. In the case of aromatic PNC, no hydrolytically unstable products are formed, and PNC cannot be reduced *via* this mechanism.

It has previously[17] been shown that the barium(II) and aluminum(III) polycharged ions increase the yield of 2-amino-substituted 4-nitro- and 4,6-dinitrobenzoic acids in the monoreduction of 2,4-dinitrobenzoic and 2,4,6-trinitrobenzoic acids by $TiCl_3$. This effect can be explained[17] by the formation of a complex between the ionized carboxyl group of RA and polycharged cations or a chelate involving both the *o*-nitro group and ionized carboxyl group and metal cations. As indicated above, alkali-earth metal cations have no effect on the reduction rate of TNT by the titanium(III) ions. The preparative reduction of TNT with the titanium(III) ions in the presence of the barium salt showed that the barium(II) ions did not affect the regioselectivity of the process. Thus, the considered phenomenon differs from the described interpretation of reduction of nitrobenzoic acids.

In the presence of $CuCl_2$, as in the case of $FeSO_4$, the reaction between the titanium(III) salt and TNT is accelerated and the content of *ortho*-isomer **1** in the reaction mixture increases remarkably (Fig. 2). In this case, regioselectivity increases to a greater extent than in the reaction with $FeSO_4$: its content increases from 25 to 70%.

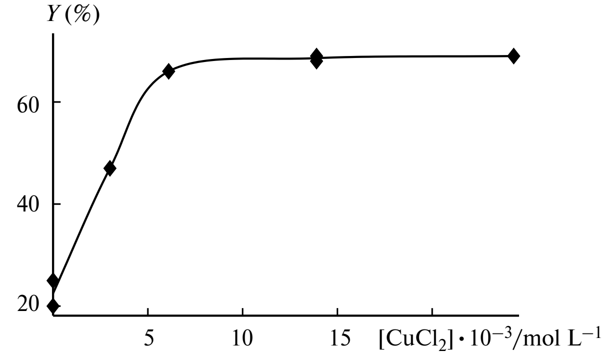


Fig. 2. Relative content of 2-amino-4,6-dinitrotoluene (**1**) (Y) in mixture **1**—**2** for the partial reduction of TNT (C = 0.04 mol L^{-1}) with $TiCl_3$ *vs.* $CuCl_2$ concentration in a reaction mixture (85 vol.% MeOH) containing 3% HCl (concentration of $TiCl_3$ 0.09 mol L^{-1}, TNT conversion 30—50%, 20—25 °C).

The general character of this activation of the *o*-nitro groups by the iron salts was confirmed by a similar reaction of 2,4-dinitrochlorobenzene. In the presence of $FeSO_4$ (0.609 mol L^{-1}) and keeping other conditions unchanged, the content of forming 2-amino-4-nitrochlorobenzene increased from 31 to 54% (at 30% conversion of dinitrochlorobenzene).

Three mechanisms can be responsible for a change in the regioselectivity of reduction of aromatic PNC by the titanium(III) and vanadium(II) salts in the presence of iron(II) or copper(II) ions.

I. Intermediate formation of binuclear complexes, whose reactivity is higher than that of the starting reactants, due to the reaction of $TiCl_3$ and $FeCl_2$ (or $CuCl_2$). However, the redox potential of the Ti^{3+}/Ti^{4+} system remains unchanged when an iron salt is introduced, which excludes the acceleration of aromatic PNC reduction by the titanium(III) ions in the presence of low concentrations of the iron(II) or copper(II) ions *via* this mechanism. In addition, ions with a higher oxidation state are characterized by the formation of polynuclear complexes.

II. Formation of a complex between metal ions and RA of nitro compounds generated by the electron transfer from the titanium(III) ion to the substrate. In this case, the distributions of a charge and lone electron spin density in the RA should change. These parameters are known[4] to determine the direction of RA protonation reactions and, as a consequence, regioselectivity of the process. In a more general form, the formation of a complex between an RA and M^{2+} ion changes the reactivity of the RA at two reaction centers. For instance, the *p*-nitro group as a less sterically hindered center is predominantly involved in complex formation, and protonation proceeds mainly at the free *o*-nitro group of the RA, which should increase the content of isomer **1** over **2**.

III. Formation of a complex between a metal ion and the starting nitro compound. In this case, the electron transfer to this complex produces the same complex $RA \cdot M^{2+}$ as that *via* mechanism II after complex formation of the RA with metal ions. Mechanisms II and III are presented in Scheme 1 for TNT, where M^{2+} is a metal ion (iron(II) or copper(II)), and the reaction products are mixtures of isomers **1** and **2** of different compositions formed by the protonation of the RA and RA complexes with the metal ions, respectively.

According to Scheme 1, an increase in the concentration of the bivalent metal ions in a solution should be accompanied by an increase in the concentration of RA complexes with such cations, whose protonation yields a mixture of isomers with a higher content of compound **1**. The curves of the dependence of the isomeric composition of the reduction products on the metal ion concentration reach a limit (see Figs 1 and 2) corresponding to the predominant occurrence of the process *via* route *b*. A change in the regioselectivity of reduction is much more sensitive to the presence of iron(II) ions in the solution than the acceleration of the process by these ions. In particular, the isomeric composition of the reduction products of TNT by the titanium(III) ions stops depending on the concentration of the latter exceeding 0.01 mol L^{-1} (see Fig.1, curve *1*). At the same time, for a given concentration of the iron ions, the process rate increases twofold, while the 6—8-fold acceleration of the reduction needs very high concentrations of the iron ions: 0.2—0.3 mol L^{-1}.[9,10] This difference in character of the dependence of the reduction acceleration and regioselectivity of the process on the metal ion concentration can indicate differences in mechanisms of these phenomena.

The reactions of TNT (or its complex with metal ions) with the titanium(III) ions are presented in Scheme 1 as irreversible, although the redox electron transfer processes can be reversible. In our opinion, under the experimental conditions (acidic aqueous-alcohol solutions), protonation rates of RA (or their complexes) are so high that their concentration in a solution is very low, and these reactions should be virtually irreversible. However, in this case, the acceleration of reduction *via* mechanism II cannot be explained, because RA complexes with metal ions are formed after the irreversible reaction. At the same time, the complex formation of a nitro compound with metal ions followed by the electron transfer *via* mechanism III makes it possible to explain both the acceleration of reduction and the change in regioselectivity of the process in the presence of the iron(II) or copper(II) ions. However, this mechanism does not explain the aforementioned difference in influence of the metal ions on the acceleration of the reaction and its regioselectivity. Therefore, we believe that the acceleration of the process can be related to the formation of a complex of the nitro compound with metal ions and their higher reduction rate (mechanism III), and the change in regioselectivity is caused by the reaction occurrence *via* mechanisms II and (in part) III. A higher complexing ability of an RA compared to neutral nitro compounds should result in a change in regioselectivity at rather low concentrations of metal ions when their influence on the kinetics of the process is relatively low.

Finally, we would like to mention an analogy of the phenomenon considered to the reduction of PNC by hydrazine hydrate or using catalytic hydrogenation. In the absence of iron compounds, the reduction of aromatic PNC using these methods affords mainly *para*-isomers,[18,19] whereas the amount of *ortho*-isomers increases sharply in the presence of iron hydroxide or iron salts.[18] As shown above, the copper salt exerts a similar effect on the regioselectivity of reduction by the titanium(III) ions. However, this effect is stronger than in the case when the iron salt is used. Although the mechanisms of the compared methods differ, the *ortho*-orienting influence of the copper compounds on catalytic hydrogenation or reduction by hydrazine cannot be excluded.

To conclude, we found that the regioselectivity of TNT reduction with titanium(III) or vanadium(II) ions in the presence of the iron(II) salts can be varied in a wide range.

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