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ORIENTATION OF BENZOPHENONE DINITRO DERIVATIVES MONO-REDUCTION

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Abstract. *The paper presents a study of monoreduction selectivity process of 3,4'-NO_2-4-R-benzophenones containing different functional groups. The presence of an electron-accepting substituent in the ortho-position of the nitro group facilitated its reduction, while electron-donating and bulk functional groups prevented it.*

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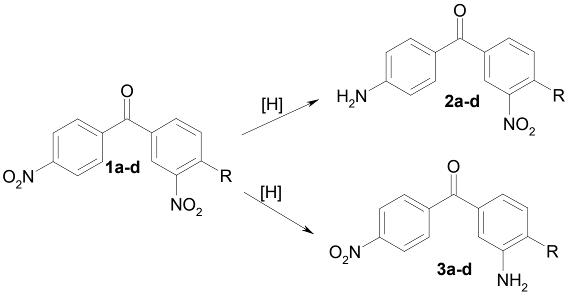
Introduction

Aromatic aminonitro compounds are widely used by many industries to produce high quality dyes, polymeric materials (polyanilines), liquid crystal devices and displays, explosives, pharmaceuticals, and agricultural preparations [1-6]. The one of the most promising methods for the synthesis of bendamustine is based on the use of 2-chloro-5-nitroaniline [7].

Reaction of mono-reduction of one of several NO_2-groups in polynitroaromatic compounds is the most important method for the preparation of aminonitroarenes [8]. A number of successful examples of using this method for the synthesis of nitroanilines have been reported in the literature [9-14]. However, the formation of a mixture of isomers has been reported in a large number of papers [15-19]. Therefore, the question of which of the several non-equivalent nitro groups in polynitrosodiennes will be reduced first is still of great importance for a large number of compounds. There is a lack of available data on the mono-reduction of polynuclear dinitroarenes containing nitro groups in different cycles in the literature. These nitroanilines are in demand by the textile industry as dyes with high performance characteristics, including fungicidal activity. Therefore, this study considers the selectivity of dinitro derivatives mono-reduction process as an interesting class of isolated polycyclic compounds of unsymmetrical benzophenones.

The main part

We chose 3,4'-NO_2-4-R-benzophenones containing different substituents in the *ortho*-position to one of the nitro groups, which had different electronic and spatial effects. The reducing agent was tin(II) chloride. It allowed us to perform an efficient synthesis of amino compounds in acid medium [20]. The criterion for evaluating the mono-reduction selectivity reaction **1** was the ratio of the resulting nitroamines **2** and **3** (Fig. 1). It can only be used if there is no diamine compound in the reaction mixture. Otherwise, we can not define the particular isomer consumed for its formation. Therefore, we preliminarily developed a procedure for the mono-reduction reaction, which excludes the formation of diaminobenzophenone (see experimental part).



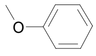
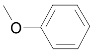
R= a) Cl, b) CH_3, c) OCH_3, d) 

Fig. 1. Direction of the reduction reaction of the nitro group

We determined the ratio of products **2** and **3** as the peak areas ratio of these compounds proton signals in the ^1H NMR spectrum. The signal of the amino group protons doubled intensity as the characteristic signal was recorded in the strong-field region of the spectrum (Table 1).

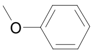
Table 1. Values of amino group proton signals in the ^1H NMR spectrum of the reaction mixture of 3,4'-NO_2-4-R-benzophenone mono-reduction products **1a**-**d**

№	R	Values of amino group proton signals: δ, m.d.	
		Isomer **2**	Isomer **3**
1	Cl	6,27	5,35
2	CH_3	5,75	4,69
3	OCH_3	6,12	5,14
4		6,15	5,32

The proton signals of the amino groups came out on the ^1H NMR spectrum in accordance with the screening effect and the position of the substituents. The absorption band of the amino group located on the *p*-position to the electron acceptor carbonyl group always came out in the weaker region of the spectrum compared to the *m*-position.

Table 2 shows the monoreduction of 3,4'-NO_2-4-R-benzophenones **1** (**a**-**e**).

Table 2. Ratio* of the products of the mono-reduction reaction of 3,4'-NO_2-4-R-benzophenones **1a**-**d** ([Substrate]:[$SnCl_2 \cdot 2H_2O$]=1 : 3, 70 °C, 40 min)

№	R	Ratio of isomers **2/3**
1	Cl	0,22
2	CH_3	1,73
3	OCH_3	2,36
4		6,01

*according to ^1H NMR spectroscopy

Table 2 shows the mono reduction of 3,4'-NO_2-4-Cl-benzophenone (**1a**), which to a greater extent is resulting with the formation of nitroaminoproduct **3a**. The 4'-nitro group was reduced preferentially in other compounds **1b-d** containing electron-donating substituents in the *ortho*-position of the nitro group. The amount of nitroamine **2** increased with increasing volume of substituent R.

Based on the data obtained we can conclude the presence of the electron acceptor substituent (Cl) at the *ortho*-position to the nitro group. It promotes its reduction whereas the electron donor and bulk functional groups prevented it. Therefore, we can expect the mono-reduction of asymmetric 4-R-4'-R1-3,3'-dinitrobenzophenones, where R and R1 are electronically different substituents. Indeed, the nitro group present in the more electron-deficient fragment of the molecule should be reduced first.

Our assumption was confirmed by the reduction of 4-chloro-4'-methyl-3,3'-dinitrobenzophenone (Fig. 2). Only one product was isolated from the reaction mass. It was identified as 4-chloro-3-amino-3'-nitro-4'-methylbenzophenone (see experimental part).

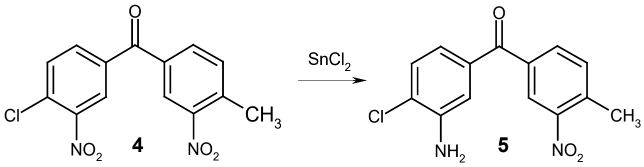
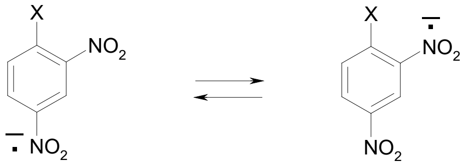


Fig. 2. Reduction reaction of the nitro group in 4-chloro-4'-methyl-3,3'-dinitrobenzophenone

Quantum-chemical modelling of the dinitrobenzophenone anion radicals protonation process was conducted to explain the results of experiments on the reduction selectivity of asymmetric dinitrobenzophenones. This stage determines the dinitroarenes orientation of the mono-reduction process. Therefore, [21] shows the dinitrosubstrate anion radical is the key particle influencing the orientation of selective reduction of unsymmetrical dinitroarenes. The use of 1-substituted 2,4-dinitrobenzenes labeled with ^{15}N isotope for the *ortho*-nitro group made it possible to show their anion radicals exist in protonic media in two forms characterized by the preferential localization of spin density on the *ortho*- or *para*-nitro group (Fig. 3). Accordingly, the nitro group on which the spin density is localized will be protonated first. It is in agreement with the direction of dinitrosubstrates partial reduction.



where X=CH_3, OH, Cl, Et, i-Pr, NEt_2

Fig. 3. Two forms of radical anion for 1-substituted-2,4-dinitrobenzene

Similar to the mononuclear benzoyl structures, there are two forms of anion radicals for benzophenones: *meta*- and *para*- according to the position of the corresponding nitro group to the carbonyl one (Fig. 4).

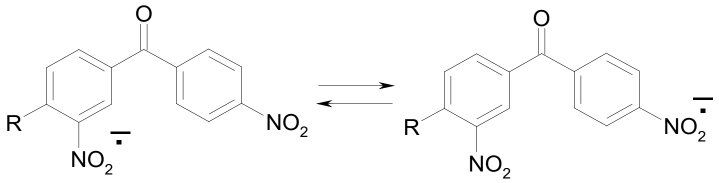


Fig. 4. Two anion-radical forms for substituted 3,4'-dinitro-4-R-benzophenones

Data on geometry and energy of the anion radical of 3,4'-dinitro-4-methylbenzophenone chosen as a model object for study were the results of quantum-chemical calculations using the PM3 method (MOPAC 7.00 software package).

Analysis of the anion radical geometry showed the presence of the particle non-coplanar structure with strongly differing spatial arrangement of the aromatic rings in terms to the plane of the carbonyl group. The arrangement of the nitro groups in terms to the planes of the phenyl nuclei associated with these nitro groups also varies (Fig. 5).

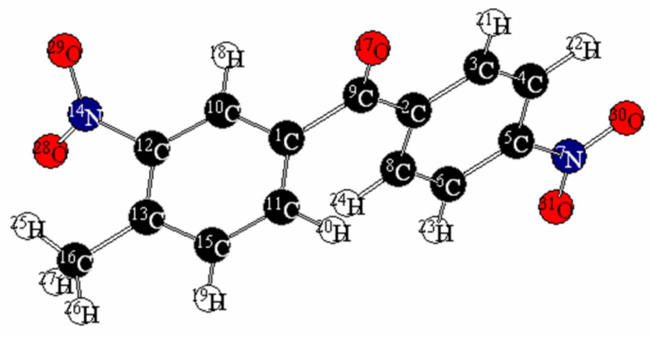


Fig. 5. Geometry of the 3,4'-dinitro-4-methylbenzophenone anion radical

The aromatic rings of the anion-radical structure are arranged in space with one nucleus (containing a nitro group in the *para*-position) almost in the plane of the carbonyl fragment and the other nucleus rotated through almost 90° relative to the plane of the CO-group. The atoms of the nitro group at the *para*-position relative to the carbonyl group do not extend out of the plane of the phenyl ring. At the same time, the second nitro group is arranged with the oxygen atoms outside the plane of the benzene ring to which the functional group is linked, following a rotation around the C-N bond. The value of the angle between the planes considered as 55.8°.

We can observe some differences for the N-O bond lengths of the anion-radical nitro groups. In the nitro group located in the *meta*-position to the carbonyl fragment the values of this parameter are 1.21694 and 1.21580 Å, higher values of N-O bond lengths in the *para*-positioned nitro group are 1.23166 and 1.23214 Å.

Also we simulate the protonation processes of two possible forms of the anion radical model compound. Since the reduction process was conducted in an acid-alcohol solution, the protonating agent was a protonated alcohol, for example - $CH_3O^+H_2$.

The geometrical parameters of the protonated particles are shown on Fig. 6 and 7 for two forms of protonated anion radicals, respectively.

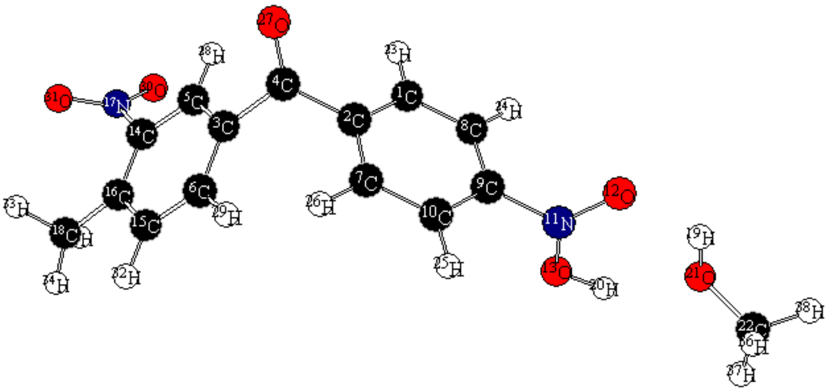


Fig. 6. Geometric parameters of the 3,4'-dinitro-4-methylbenzophenone anion radical protonated at the *para*-nitro group

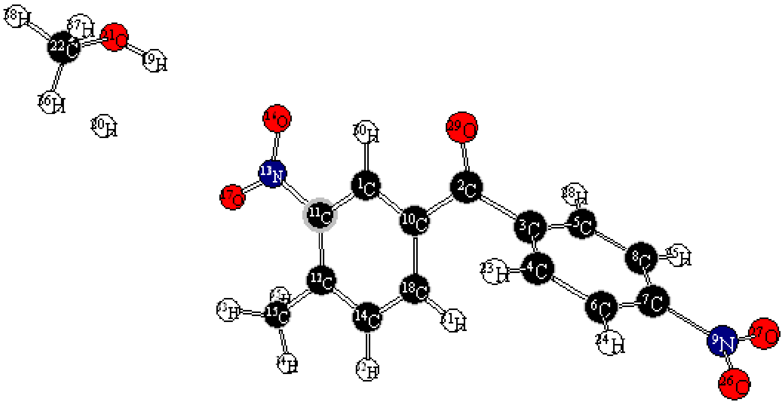


Fig. 7. Geometric parameters of the 3,4'-dinitro-4-methylbenzophenone anion radical protonated at the *meta*-nitro group

Figure 6 and 7 show the geometry of the structures formed by protonation changes compared to the anion radical.

Changes of geometrical parameters in the process of protonation of anion-radical particles testify to the level of those energy costs necessary to perform these transformations. The more significant these transformations of the particle structure are, the higher the energy costs, and the less probable is the formation of such particles.

The probability of *meta*-protonated structure formation is lower for the considered example with protonation of 3,4'-dinitro-4-methylbenzophenone anion-radical. It is confirmed by the calculated thermodynamic value of heat formation equal to -5.43576 kcal/mol. For *para*-protonated form of anion-radical the value of heat formation is lower and is -52.10320 kcal/mol. There is thermodynamic reaction control.

A comparison of the O-H bond lengths values formed by protonation also indicates a higher probability of *para*-protonated particle formation. In this case the bond length is 0.9 Å, while in the case of *meta*-protonation the bond length is 2.6 Å.

Thus, the computer simulation data agree well with the experimental results on the mono-reduction process of non-symmetrical dinitrobenzene.

Experimental part

We determined the melting points on a PolyTherm A device at a heating rate of 3 °C/min and did not adjust. We recorded NMR spectra on a Bruker DRX-400 for DMSO-d6 solutions.

The remaining solvent proton signals in ^{1}H NMR (δ 2.50 ppm) were used as the reference for the chemical shift counts. Mass spectra were recorded on a FINNIGAN MAT instrument. INCOS 50, electron flux energy 70 eV.

General methodology for mono-reduction of asymmetrical benzophenones 1a-d. Solutions of 0.003 mol dinitrosubstrate **1a-d** in 50 ml propanol-2 and 0.009 mol $SnCl_2 \cdot 2H_2O$ in 50 ml 18% HCl were synchronously added through droplet funnels for 30 min in a flask containing 15 ml propanol-2 heated to 70 °C. Then the reaction mixture was stirred for further 10 min at 70 °C. The products were isolated by treating the reaction mixture with 25% ammonia solution to pH = 7-8 and extracting with several portions of chloroform (Σ= 400 ml), which was then removed under reduced pressure.

4-Chloro-3-amino-3'-nitro-4'-methylbenzophenone: yield 94.5%, T. melt. 111-112 °C. ^{1}H NMR spectrum (DMSO-d_6), δ, m.d. (*J*, Hz): 8.24 c (1H, $H^{2'}$), 7.88 dd (1H, $H^{6'}$, 6.0, 1.0), 7.69 d (1H, $H^{5'}$, 7.0), 7.37 d (1H, H^5, 7.0), 7.22 d (1H, H^2, 1.0), 6.89 dd (1H, H^6, 6.0, 1.0), 5.70 s (2H, NH_2), 2.57 s (3H, CH_3). Mass spectrum, m/z ($I_{relative}$, %): 291 (100) $[M]^+$, 156 (58), 154 (90), 126 (68), 90 (69). Found %: C 57.61; H 3.99; N 9.79. $C_{14}H_{11}ClN_2O_3$. Calculated %: C 57.84; H 3.81; N 9.63; M 290.70.

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