Aromatic Nucleophilic Substitution (S_NAr) Reactions of 1,2- and 1,4-Halonitrobenzenes and 1,4-Dinitrobenzene with Carbanions in the Gas Phase

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In the gas-phase reactions of halonitro- and dinitrophenide anions with X (X = F, Cl, Br, NO_2) and NO_2 groups in *ortho* or *para* position to each other with selected C-H acids: CH_3CN, CH_3COCH_3, and CH_3NO_2, products of the S_NAr-type reaction are formed. Nitrophenide anions are generated by decarboxylation of the respective nitrobenzenecarboxylate anions in ESI ion source and the S_NAr reaction takes place either in the medium-pressure zone of the ion source or in the collision chamber of the triple quadrupole mass spectrometer. In the case of F, Cl, and NO_2 derivatives, the main ionic product is the respective $[NO_2\text{-}Ph\text{-}CHR]^-$ anion (R = CN, $COCH_3$, NO_2). In the case of Br derivatives, the main ionic product is Br^- ion because it has lower proton affinity than the $[NO_2\text{-}Ph\text{-}CHR]^-$ anion (for R = CN, $COCH_3$). For some halonitrophenide anion C–H acid pairs of reactants, the S_NAr reaction is competed by the formation of halophenolate anions. This reaction can be rationalized by the single electron-transfer mechanism or by homolytic C–H bond cleavage in the proton-bound complex, both resulting in the formation of the halonitrobenzene radical anion, which in turn undergoes $-NO_2$ to $-ONO$ rearrangement followed by the $NO^.$ elimination.   (J Am Soc Mass Spectrom 2007, 18, 1351–1363) © 2007 American Society for Mass Spectrometry

Aromatic nucleophilic substitution (S_NAr) reactions are important from both practical and theoretical point of view [1–4]. Typical S_NAr reactions (in solution) proceed according to the mechanism shown in Scheme **1**.

In the first step a σ^X-adduct is formed, which eliminates the X group (usually halogen) leading to the final product. Stable, resonance-stabilized σ-adducts can be formed only in positions *ortho* and *para* to the nitro group, so only *ortho-* and *para*-halonitrobenzenes undergo S_NAr reaction.

Aromatic nucleophilic substitution reactions have also been studied in the gas phase. Early findings in this field were reviewed by Bowie [5]. More references can be found in the reviews on gas-phase anion chemistry by Squires [6], Gronert [7], and DePuy [8, 9]. Only in a couple of the published works on the gas-phase S_NAr reactions aromatic nitro compounds were used as the electrophilic substrates. In 1975, a short communication from Briscese and Riveros described a series of gas-phase reactions of halobenzenes with alkoxide anions and they mentioned (in a footnote) that also *p*-nitrofluorobenzene enters the nucleophilic displacement reaction [10]. Two years later Bowie and Stapleton described the gas-phase S_NAr reaction between *o*-dinitrobenzene and chloride anions which proceeded in the ICR cell [11]. Since that time gas-phase ion-molecule reactions involving aromatic nitrocompounds were not investigated until the beginning of the 21st century when such studies were started in the laboratories of R. Graham Cooks and ours (wide infra). Also, Riveros and coworkers published a short communication in which they described quite unusual gas-phase substitution of the nitro group in nitrobenzene with fluoride anion [12]. It should also be mentioned that in their paper, Riveros et al. finally corrected the PA value of the nitrophenide anion, which they found to be equal to 374 ± 3 kcal/mol, about 16 kcal/mol higher than the value measured by Meot-ner and Kafafi in 1988 [13].

Much more work has been done on the gas-phase aromatic substitution reactions in halobenzene derivatives. Early works on this subject were published by Briscese and Riveros [10], Dzidic et al. [14], and by Sullivan and Beauchamp [15]. Many more comprehensive studies were performed in Nibbering's group
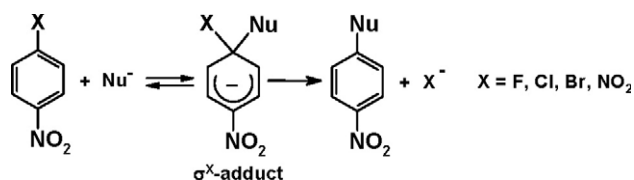
Scheme 1. Mechanism of the S_NAr reaction.

[16–19]. In the series of papers they described the reactions of halophenyl alkyl ethers as well as hexafluorobenzene with a variety of nucleophiles. In all cases, at least some of the reaction products were formed via S_NAr reactions. The theoretical study of the mechanisms of the aromatic nucleophilic substitution in the gas phase was published by Simkin et al. [20]

During the last few years, a series of papers from Cooks' laboratory dealing with the reactions of aromatic nitro compounds with nucleophiles in a gas phase have been published [21–23]. In these papers the authors proved that it is possible to record mass spectra of the gas-phase σ-adducts of many aromatic nitro compounds with carbanions generated from nitromethane, acetone, and acetonitrile. These carbanions were generated using CI or APCI ionization methods. The results presented in all three papers showed that, for some nitro compounds, S_NAr reactions were observed. Surprisingly, this term was not explicitly used and, in the case of results described in the first of the cited papers [21], the rationalization of results was incorrect from our point of view. This problem will be discussed in detail later in this paper.

In our laboratory, we have developed simple and efficient method for generating gas-phase phenide anions with various substituents in the ring [24]. The formation of these anions can take place in the medium pressure part of the ESI ion source or in a collision cell (for diagram and description see reference [25]). It is possible also to subject these anions to reactions with various gas-phase reagents, which are introduced with the curtain or collision gases.

We have found that di- and trinitrophenide anions (generated by decarboxylation of the respective nitrobenzoic acids anions in the ESI ion source) can react with C–H acids with proper acidity yielding anionic σ-adducts [25]. However, we were not able to observe σ-adducts containing one nitro group. To increase the electrophilicity of the aromatic ring and stabilize the σ-adduct we decided to introduce a halogen substituent on the ring. We expected also that in the case of compounds with a halogen substituent in the *ortho* and *para* positions relative to the nitro group, S_NAr-type reaction could be observed. It is important to mention that at the time that we started our work, the papers by Cooks et al. [21–23] had not been published.

In the present paper, we describe the results obtained for the reactions of various halonitrophenide and dinitrophenide anions generated from the respective halonitro- and dinitrobenzoic acids with gas-phase C–H

acids like acetone, acetonitrile, and nitromethane. We discuss also some results described by Cooks et al. [21], giving them a new rationalization.

Experimental

All experiments were performed using an API 365 triple quadrupole mass spectrometer (MDS Sciex, Toronto, Canada) equipped with a TurboIonSpray electrospray ion source. This source was operated in a standard ESI mode, i.e., without additional drying gas. Reagents and solvents (HPLC grade) were commercially available or were synthesized according to known procedures.
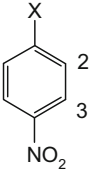
Nitrobenzoic acids were infused into the ESI ion source as $\sim 1 \times 10^{-4}$ M solutions in MeOH at a 5 to 10 μL/min rate. Ion source parameters were set as follows: capillary voltage -4 kV, nebulizer gas 12 and curtain gas 8 (arbitrary units, N_2 in both cases). The entrance ion optics voltages were optimized for the maximum production and transmission of the ions of interest. Typical declustering potential (DP) values were between 20 and 40 V, and focusing potential (FP) values between 180 and 300 V.

Saturation of the curtain gas with the reagents vapors was achieved by injecting liquid reagent using a T-connector directly into the stream of nitrogen with a syringe pump at a flow rate of 5 μL/min.

To enable the use of different collision gases, the collision gas inlet has been modified to allow introduction of the selected collision gas independently from the curtain gas. For the CID experiments nitrogen was used as a collision gas. For studying the ion-molecule reactions in the collision cell, a stream of nitrogen was flushed over the surface of the appropriate liquid reagent in a small flask. It was not possible to estimate the concentration of the reagent vapors in nitrogen, however, for qualitative experiments this parameter was not important. The pressure of the collision gas has been set at 3 (arbitrary units) which, according to the manufacturer's specification, corresponds to a pressure of approx. 3×10^{-3} mbar. Collision cell parameters were set as follows: entrance potential (CEP) -10 V, exit potential (CXP) 15 V. Collision energy (CE) has been adjusted manually in the range between 5 and 30 eV (laboratory frame) to achieve the best results. Usually, ion-molecule reactions in a collision cell were performed at the lowest possible collision energy (5 eV).

Density functional theory (DFT) calculations were performed using a hybrid B3LYP functional at the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d) level with the Gaussian 98 program package [26]. The same program was also used for G3(MP2) and HF calculations. HF calculations were performed on the 6-31G(d) level. Transition-state geometry was optimized using the QST3 algorithm. Proton affinities (PA) are given in kcal/mol (1 kcal/mol = 4.184 kJ/mol). For brevity, PA values of the conjugate bases of C–H acids will be denoted as PA_{CB}.

Table 1. Proton affinities of the conjugate bases (PA$_{CB}$) of selected compounds discussed in this work

Compound	PA$_{CB}$ experimental[a] [kcal/mol]	PA$_{CB}$ calculated [kcal/mol]
X = F, pos. 2	—	371[b]
X = F, pos. 3	—	375[b]
X = Cl, pos. 2	—	371[b]
X = Cl, pos. 3	—	373[b]
X = Br, pos. 2	—	369[b]
X = Br, pos. 3	—	371[b]
X = NO$_2$, pos. 2 and 3	—	365[b]
p-NO$_2$-Ph-CH$_2$CN	329	—
CH$_3$NO$_2$	356.4–358.0	358[c]
CH$_3$COCH$_3$	367.6–369.6	369[c]
CH$_3$CN	366.6–374.8	372[c]
HF	371	—
HCl	333	—
HBr	324	—
HNO$_2$	340	—

[a]Data taken from NIST database [27].
[b]Calculated using B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d) method.
[c]Calculated using G3(MP2) method.

Experimental PA values were taken from the NIST database available on the Internet [27].

Results and Discussion

Before starting the experiments we decided to perform a number of proton affinity calculations to see which pairs: halonitrophenide anion-C–H acid would be expected to form a stable σ-adduct, taking into account the rules established by us in our previous work [25]. We found that the PA value of the nitrophenide anion should be lower than that of the C–H acid anion by no more than about 13 kcal/mol. Endothermicity of the proton transfer reaction between the nitrophenide anion and the C–H acid was required to stabilize the resulting ion-molecule complex and, finally, the σ-adduct. When the difference in PA values was too high, no reaction occurred. On the other side, when the proton transfer step of the reaction was exothermic, the only ionic product was the anion of the C–H acid. We expected that the formation of the relatively stable σ-adducts would be required also for S$_N$Ar reactions so the thermochemical relations described above should be observed also in this case.

All PA data for the conjugate bases of compounds we were interested in are collected in Table 1. There were no experimental data available for p-halonitrobenzenes and p-dinitrobenzene, so we had to calculate them. Our experience, supported by an extensive comparative study of the applicability of the different calculation methods for establishing reliable PA values for medium-sized carbanions, showed that the calculations using hybrid B3LYP functional at the B3LYP/6-311+G(3df,2p)// B3LYP/6-31G(d) level should be optimal, taking into account the accuracy/calculation cost ratio. This approach usually gives PA values that differ no more than ±2 kcal/mol from the experimental data. It has to be

stressed, however, that the reliability of the experimental PA data is sometimes questionable. It can be seen, for example, for the acetonitrile anion (Table 1). The experimental PA values of this anion vary from 366.6 to 374.8 kcal/mol [27], much more than the uncertainty values given by the authors of the measurements. In contrast, calculated PA values for this anion, using a number of sophisticated compound methods such as CBS-Q, G3, G3(MP2), G3(MP2)B3LYP, which were designed to give accurate thermochemical data, as well as B3LYP with different basis sets, vary no more than 1.5 kcal/mol around the 372 kcal/mol mean value. Due to these results we decided to take calculated PA values, rather than experimental, for the anions of acetone, acetonitrile, and nitromethane.

Analysis of the data presented in Table 1 shows that the reactions between p-fluoro-, p-chloro-, and p-bromonitrophenide anions with acetone and acetonitrile should be energetically neutral or slightly exothermic. Nitromethane, due to its high acidity, should give only the proton transfer reactions with the above mentioned anions. There is a chance, however, for successful S$_N$Ar reaction or the formation of the σ-adduct when nitromethane will react with p-dinitrophenide anion.

Taking into account the results of the theoretical analysis presented above, we decided to start with the reactions of the p-fluoro-, p-chloro-, and p-bromonitrophenide anions (generated from the appropriate halonitrobenzoic acids) with acetonitrile as the C–H acid. Scheme **2** shows the reaction paths that should be expected for these reactions. Within the ion-neutral complex of p-halonitrobenzene and the carbanion, two σ-adducts can be formed: σ^H and σ^X. It is known that the formation of the σ^H-adduct is much faster [3, 4] but in this case it cannot react further. However, the formation of the σ^H-adduct is reversible, so finally σ^X-adduct is formed
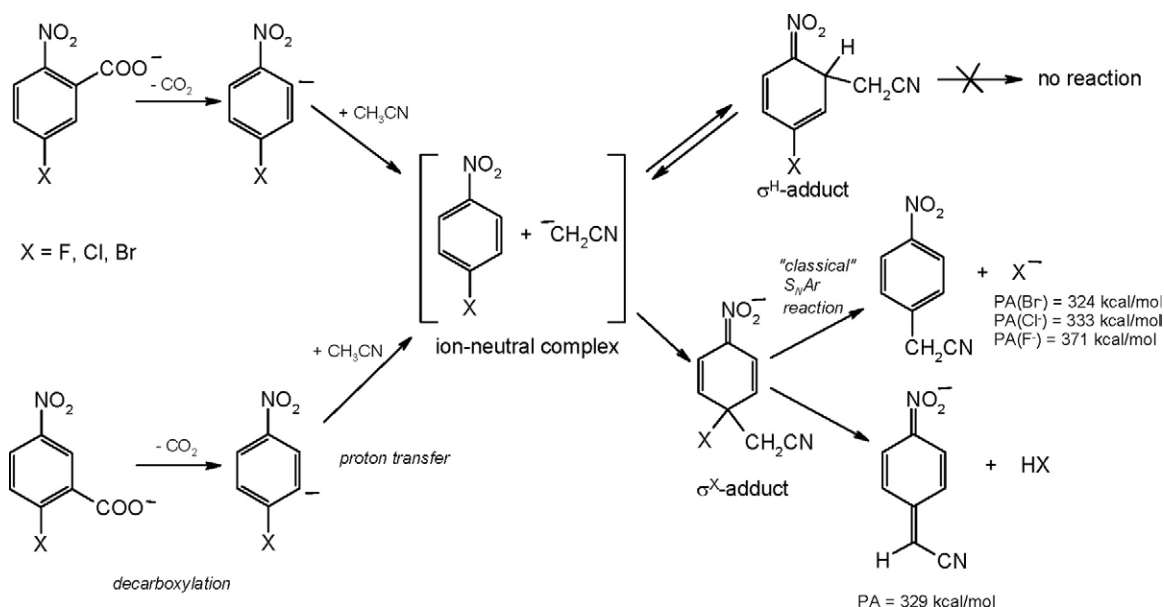
Scheme 2. Possible pathways for the reactions of 2-halo-5-nitrophenide and 5-halo-2-nitrophenide anions with acetonitrile.

that undergoes further transformations. If the reaction takes the same path as in solution, the main ionic product should be the respective halide anion. However, comparison of the gas-phase proton affinities of the halide anions and *p*-nitrophenylacetonitrile anion shows that the latter is a stronger base only in comparison with bromide anion (Scheme **2**). So, one can expect that in the reactions of fluoro- and chloronitrophenide anions with acetonitrile, *p*-nitrophenylacetonitrile anion should be the main ionic product. In the case of the bromo derivative bromide anion should be formed.

The results we obtained are in a very good accordance with our expectations. As the representative example, Q3 spectra recorded for the products of the reactions between 2-fluoro-, 2-chloro-, and 2-bromo-5-nitrophenide anions (selected with Q1) with acetonitrile in a collision cell (Q2) are presented in Figure 1a, b, and c. In the case of fluoro and chloro derivatives the main ionic product shows *m/z* 161, which corresponds to *p*-nitrophenylacetonitrile anion. We confirmed the structure of this ion by comparing CID spectrum of the *m/z* 161 ion obtained in the reaction between 5-fluoro-2-nitrophenide anion with acetonitrile in the ion source with CID spectra of model *o*-, *m*-, and *p*-nitrophenylacetonitrile (Figure 2). In contrast, for the bromo derivative, the most intense peak in the spectrum corresponds to the bromide anion. Very similar results were obtained in the reactions of 5-halo-2-nitrophenide anions with acetonitrile.

An important questions concerns the mechanism of the transformation of gaseous σ^X-adduct into final products. In the case of X = Br it was exactly the same process as observed in solution, i.e., heterolytic C–Br bond cleavage resulting in the formation of Br$^-$ anion. The formation of *p*-nitrophenylacetonitrile anion in the

case of X = F and Cl can be rationalized in two ways (Scheme **3**).

HX molecule can be eliminated in a concerted four-center mechanism or in a stepwise process which starts with the formation of the halide anion which on turn abstracts a proton from the -CH$_2$CN group. To tell more about these mechanisms we performed a series of ab initio calculations on the HF/6-31G(d) level in which we simulated the cleavage of the C–F bond. Starting from the optimized σ^X-adduct structure (Figure 3a), the C–F distance was increased in 0.3 Å steps and full geometry optimization, except of the C–F distance, has been performed each time. With increasing C–F distance, the CH$_2$CN group conformation started to change and after moving from 2.32 to 2.62 Å C–F distance the proton abstraction process was observed. Full optimization of the final structure led to the stable ion-molecule complex of *p*-nitrophenylacetonitrile anion with hydrogen fluoride molecule (Figure 3c). Interestingly, it was not possible to find a stable structure for the *p*-nitrophenylacetonitrile-fluoride anion complex. All attempts, in which F$^-$ was located close to the CH$_2$CN group, ended either with the structure (Figure 3a or Figure 3c). Consequently, the structure with the highest energy was optimized again as the transition-state (QST3 optimization method). The result is shown in Figure 3b. Calculations showed also that the activation energy of the HF elimination reaction is about 21 kcal/mol and the enthalpy of the transformation of σ^X-adduct to the *p*-nitrophenylacetonitrile anion-HF complex is about −11 kcal/mol. These very preliminary and simplified calculations show that the stepwise mechanism is quite feasible, however, the concerted process cannot be excluded. More advanced calculations are also necessary to estimate more accurate
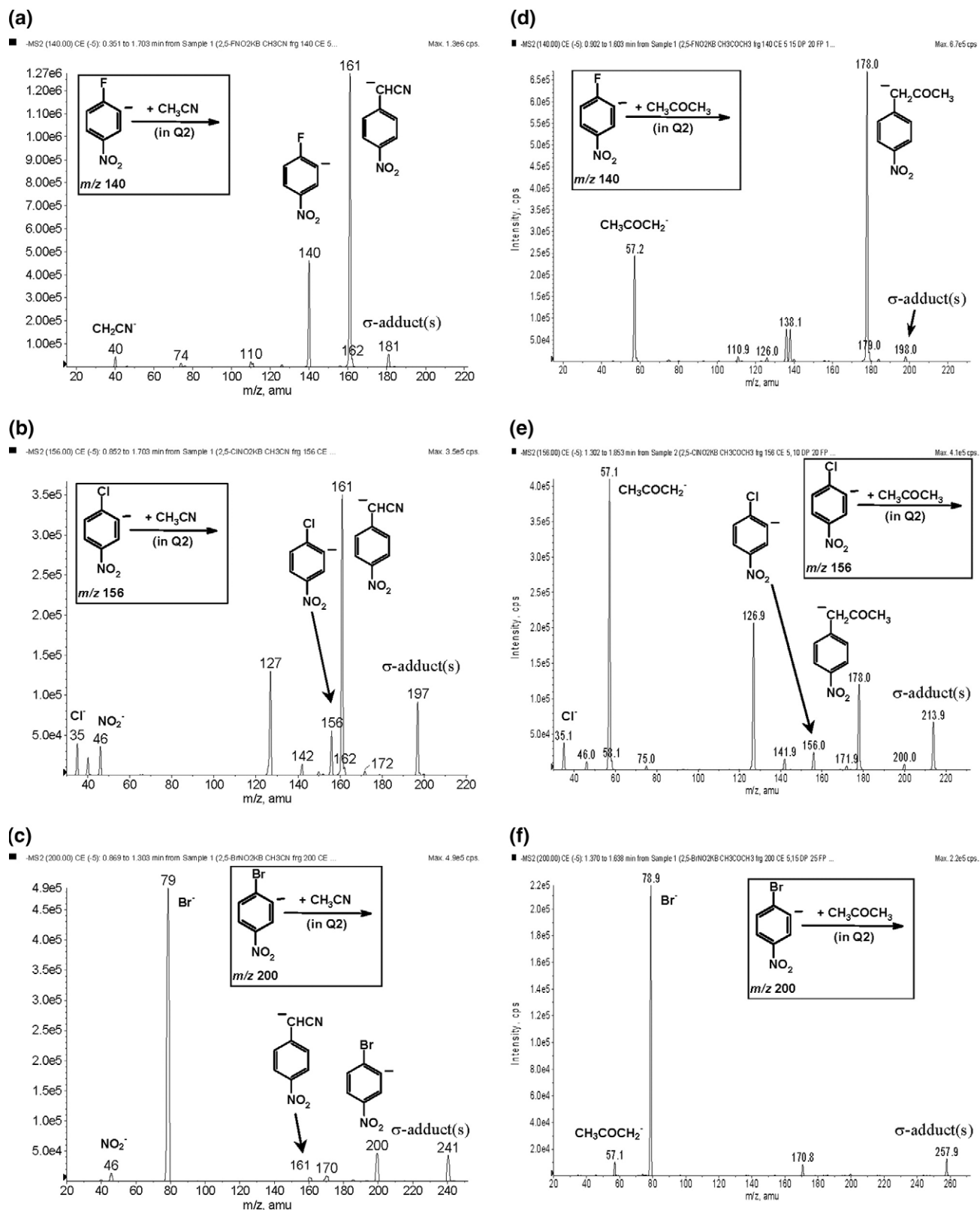
Figure 1. Q3 mass spectra recorded for the products of the reactions of (**a**) 2-fluoro-, (**b**) 2-chloro-, (**c**) 2-bromo-5-nitrophenide anions with acetonitrile, (**d**) 2-fluoro-, (**e**) 2-chloro-, and (**f**) 2-bromo-5-nitrophenide anions with acetone in a collision cell (Q2). Collision energy was set to 5 eV in all cases.
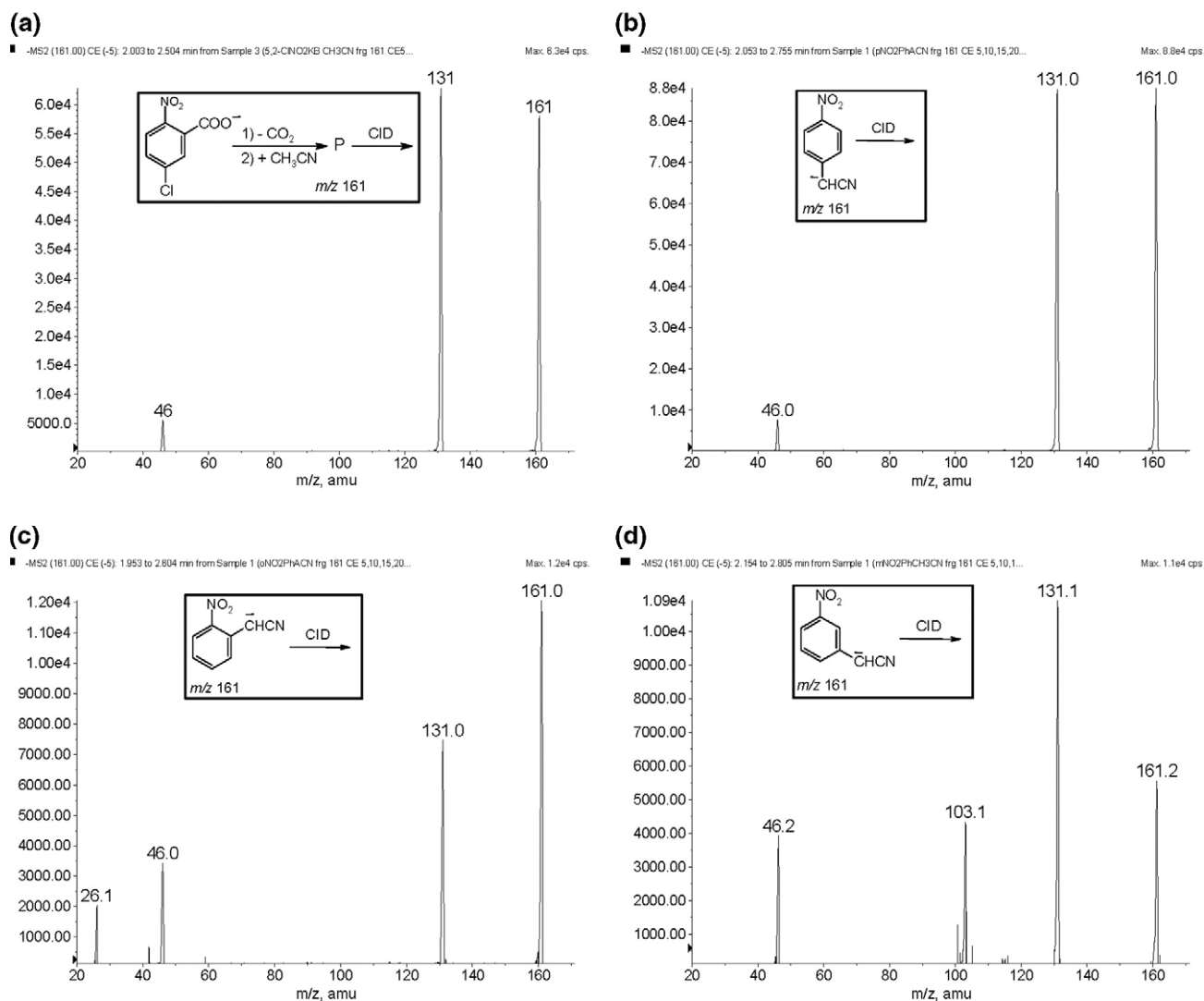
(a)

(b)

(c)

(d)

Figure 2. CID spectra recorded with the same collision energy for: (**a**) m/z 161 ion resulting from the reaction of the 5-chloro-2-nitrophenide anion with acetonitrile in the medium-pressure zone of the ESI ion source; (**b**), (**c**), and (**d**) [M − H]⁻ ion generated, respectively, from the *p*-, *o*-, and *m*-nitrophenylacetonitrile in the ESI ion source under standard conditions.

energy profiles of these processes. This work is in progress and will be published upon completion.

Both HF elimination mechanisms, i.e., concerted and stepwise, have already been proposed by other researchers. Two-step mechanism of the HF elimination from σ^X-adduct has been postulated by Nibbering et al. [16]. In their mechanism, arene-F⁻ ion-molecule complex is formed after C–F bond cleavage in the σ-adduct. This complex can undergo further transformations. As it was mentioned above, our preliminary calculations showed that such complex, in the case of compounds we were studying, is more likely the transition-state rather than the local minimum on the potential energy surface. Of course, it cannot be excluded that more advanced calculations will give different results. Concerted HF elimination mechanism has been proposed by Sullivan and Beauchamp [15]. These authors studied the reaction of tetrafluoroethylene with various nucleo-

philes and found that in the reactions with alkoxide anions CF_2CFO^- ion is formed. This result has been rationalized by a six-center or four-center concerted elimination mechanism, depending on the structure of the alkoxide anion. Stepwise mechanism has not been considered. The paper by Sullivan and Beauchamp was published in 1977, so there was no possibility to support the proposed mechanisms by calculations.

We were able to observe peaks corresponding to S_NAr reaction products also with the second tested C–H acid-acetone. The results of the reactions of 2-fluoro-, 2-chloro-, and 2-bromo-5-nitrophenide anions (selected with Q1) with acetone in a collision cell (Q2) are presented in Figure 1d, e, and f. Compared with the results of the reactions with acetonitrile, it can be seen that due to the higher acidity of acetone more intense peaks corresponding to the acetone enolate ion (m/z 57) are observed. Reaction with acetone seems also to be more
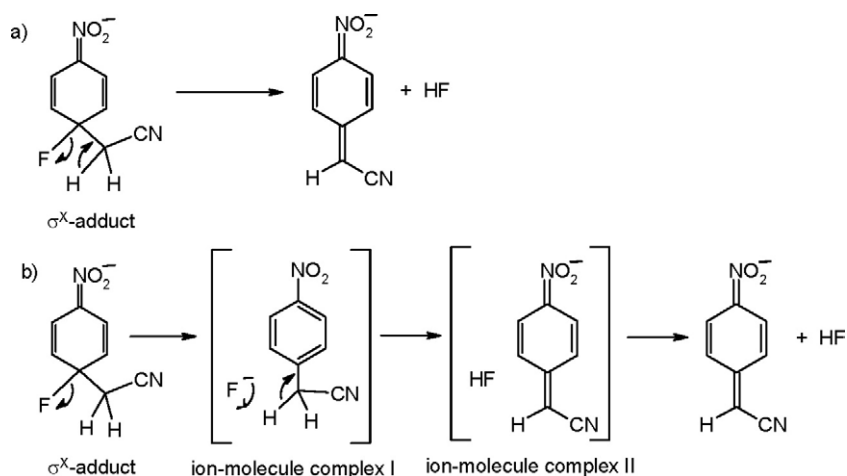
Scheme 3. Two possible mechanisms of the formation of *p*-nitrophenylacetonitrile anion and HF molecule from the σ^X-adduct: (**a**) concerted four-center mechanism, (**b**) stepwise mechanism.

efficient compared with acetonitrile, which results in the lower abundances of the reacting nitrophenide ions. This result can be again rationalized by the higher acidity of acetone, larger number of exchangeable hydrogen atoms and, possibly, better stabilization of σ-adduct and other reaction intermediates due to the larger number of degrees of freedom of acetone comparing to acetonitrile.

An interesting observation was made by careful examination of the spectrum shown in Figure 1d. The presence of *m/z* 138 peak indicates that *p*-nitrophenolate anion is formed. It was proven that it is not a fragment resulting from decomposition of the S$_N$Ar reaction product (*m/z* 178). The most likely rationalization for the formation of this ion is presented in Scheme 4.

Acetone enolate is an ambident anion so it can attach to the electrofile by the carbon or the oxygen atom. In the reactions conducted in solution at room temperature, only products resulting from the C-attack are detected. However, it was proven that at the very low temperatures, O-adducts are also observed [28]. In the gas phase, acetone enolate anion can also act as the O-nucleophile [19], so the reaction mechanism shown in Scheme 4 is possible. It has to be noted that *m/z* 138 ion

is absent in the spectrum of the products of the reaction of 2-fluoro-5-nitrophenide anion with acetonitrile. It cannot be formed in this reaction due to the lack of oxygen in the CH$_3$CN molecule. The mechanism shown in Scheme 4 follows the proposal given recently by Cooks and coworkers [22]. In their work, they observed the formation of phenolate anions in a number of reactions between nitroaromatic compounds and acetone enolate anion generated by APCI method. Of course, the elimination of HF molecule can take place also in a stepwise manner, analogously to the mechanism proposed in Scheme 3b).

p-Nitrophenolate anion was not observed in the reactions of chloro- and bromonitrophenide anions with acetone. These results may indicate that in the case of these compounds O-adducts are not formed or, more likely, they cannot decompose according to the mechanism proposed for the adduct containing the fluorine atom due to lower proton affinity of chloride and bromide anions.

In the spectra shown in Figure 1a, b, and c, peaks corresponding to the appropriate σ-adducts are also visible. In principle, two types of adducts with acetonitrile anion can be expected: σ^H- and σ^X-adducts (see Scheme 2). We tried to distinguish between these two adducts by subjecting them to CID. The results are
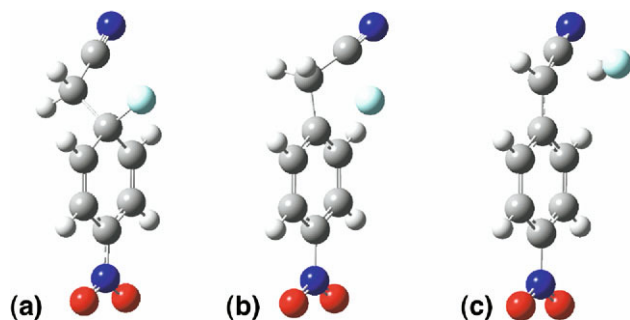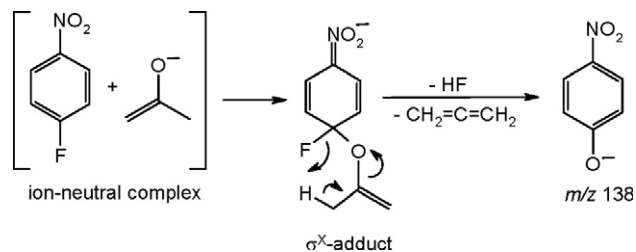

Figure 3. Optimized [HF/6-31G(d)] structures of: (**a**) σ^X-adduct of *p*-fluoronitrobenzene with acetonitrile anion (C–F bond length = 1.42 Å), (**b**) transition-state (C–F = 2.32 Å), (**c**) ion-molecule complex of *p*-nitrophenylacetonitrile anion with hydrogen fluoride molecule (C–F = 3.53 Å).

Scheme 4. Mechanism of the formation of *p*-nitrophenolate anion in the reaction between *p*-fluoronitrobenzene and acetone enolate anion. Elimination of HF molecule can proceed also by a stepwise mechanism analogous to shown in Scheme 3b.
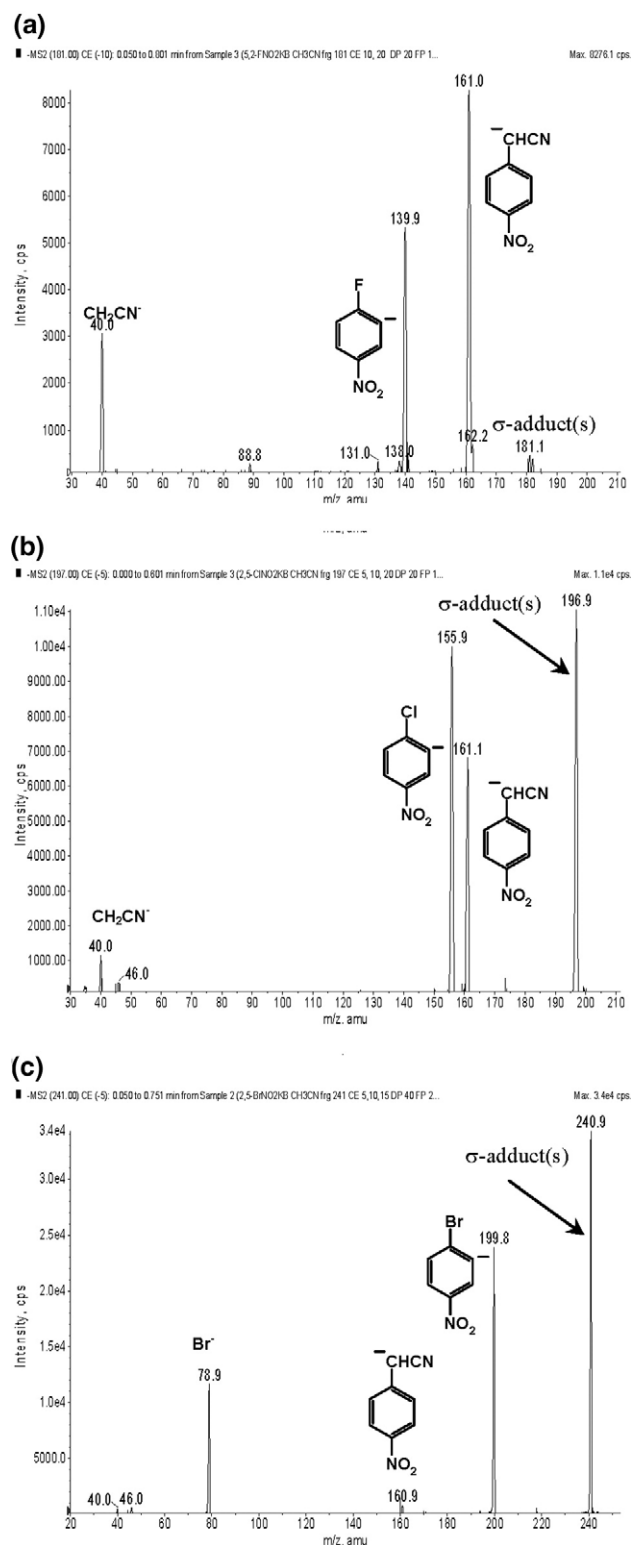
(a)

(b)

(c)

Figure 4. CID spectra recorded at the same collision energy (5 eV) of the ions corresponding to σ-adducts obtained in the reactions of: (**a**) 2-fluoro-, (**b**) 2-chloro-, and (**c**) 2-bromo-5-nitrophenide anion with acetonitrile in the ion source.

shown in Figure 4. In all three cases, two types of ionic products are observed: the S$_N$Ar reaction product (predominantly *p*-nitrophenylacetonitrile anion in the case

of F and Cl derivatives and predominantly Br$^-$ in the case of Br derivative) and respective nitrophenide anion as well as acetonitrile anion. These results show that most likely both σ^H- and σ^X-adducts are formed. Both adducts can decompose to the starting halonitrophenide or acetonitrile anions but σ^X-adduct should react also to give the S$_N$Ar products. It has also to be noted that other species such as π-complexes and proton-bound complexes (vide infra) are isomeric with the respective σ-adducts and should give similar fragmentation products. This problem can be solved theoretically by the analysis of the potential energy surface of the reaction between halonitrophenide anion and C–H acid. As it has been mentioned above, such work is under progress in our laboratory.

In contrast to the results obtained for acetonitrile, our attempts to generate σ-adducts ions with acetone in the medium-pressure zone of the ion source in the reasonable abundance failed. These experiments, in which acetone was added to the curtain gas, showed, among others, the S$_N$Ar products peaks.

S$_N$Ar reactions can proceed also with the *ortho*-substituted nitrobenzenes. To test this possibility, we performed the reactions of 3-chloro-2-nitrophenide anion (generated from 3-chloro-2-nitrobenzoate anion) with acetonitrile and acetone in a collision cell. In both cases, peaks corresponding to the respective σ-adducts as well as expected S$_N$Ar reaction products were observed. Comparison of the CID spectra of the product of the S$_N$Ar reaction with acetonitrile (*m/z* 161) with the CID spectra of three model *o*-, *m*-, and *p*- nitrophenylacetonitrile anions showed that the expected *ortho* isomer was formed. A comparison with the results obtained for isomeric anions of *ortho*- and *para*-chloronitrobenzenes showed that in the case of *ortho* isomer the relative abundance of the σ-adducts is much higher and the abundance of the S$_N$Ar reaction product, much lower than for *para* isomer. This result indicates most likely that in the case of *ortho* isomer the formation of relatively stable σ^H-adducts (mainly in a less sterically hindered *para* position to the nitro group) dominates over the formation of the σ^X-adducts. It was confirmed by the CID spectra of the σ-adduct (*m/z* 197) formed in the reaction of 3-chloro-2-nitrophenide anion and acetonitrile in the ion source. In this spectrum, *m/z* 40 and 156 peaks corresponding to acetonitrile and 3-chloro-2-nitrophenide anions dominate over the very low peak with *m/z* 161 corresponding to *o*-nitrophenylacetonitrile anion.

To be sure that we are indeed observing the S$_N$Ar reaction products, we also performed experiments with 2-chloro-4-nitrophenide anion in which halogen and the nitro group are in *meta* position to each other. It is known that in solution *m*-halonitrobenzenes do not enter the S$_N$Ar reaction so we were interested is this the case also in the gas phase. The results we obtained were generally in accordance with our expectations. In the reaction of 2-chloro-4-nitrophenide anion with acetone, both in an ion source and in a collision cell, intense peak
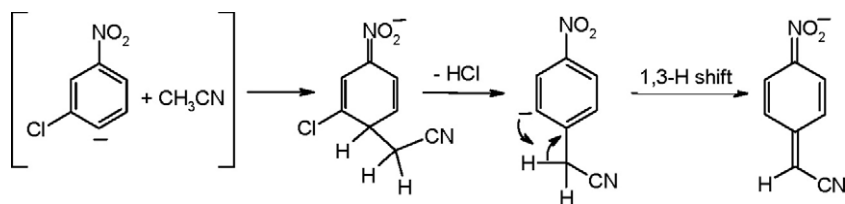
Scheme 5. Possible mechanism of the formation of *p*-nitrophenylacetonitrile anion from the σ^H-adduct formed in the reaction of 2-chloro-4-nitrophenide anion with acetonitrile.

corresponding to the respective σ-adduct (*m/z* 214) was observed and *m/z* 187 peak corresponding to HCl elimination from the σ-adduct was absent. Somewhat confusing were the results of the reaction of 2-chloro-4-nitrophenide anion with acetonitrile. In this case also the intense peak corresponding to respective σ-adduct (*m/z* 197) was observed but it was accompanied by a very weak but still visible *m/z* 161 peak corresponding to the HCl elimination from the σ-adduct. We tried to establish the structure of *m/z* 161 ion by performing CID experiment. Due to the very low abundance of the parent ion, the results are not 100% clear but the spectrum we obtained is most similar to that of the *p*-nitrophenylacetonitrile anion. Neither *m/z* 26, characteristic for the *ortho* isomer, nor *m/z* 103 peaks observed for the *meta* isomer were present in the spectrum. In our opinion, these results show that, indeed, *m*-halonitrobenzenes do not enter the S$_N$Ar reactions in the gas phase. It has to be noted, however, that according to the results obtained with acetonitrile, HCl elimination from the σ^H-adduct cannot be completely excluded. It can proceed according to the mechanism presented in Scheme 5. When the σ-adduct is formed in position *ortho* to the halogen and *para* to the nitro group, HCl elimination followed by the 1,3-proton shift can occur, leading finally to *p*-nitrophenylacetonitrile anion.

In the spectra obtained for the reactions of halonitrophenide anions with C–H acids (acetone, acetonitrile) in a collision cell, strange peaks appear at *m/z* 111 for fluoro- and *m/z* 127/129 for chloronitrophenide anions, independently of the type of the C–H acid (see Figure A). In some instances, their intensity was quite high as, for example, in the reaction

between 2-chloro-5-nitrophenide anion with acetonitrile or acetone (Figure b and c). From the experiments with chloronitrophenide anions, it was clear that these ions contain halogen atom and, due to their odd *m/z* values, they do not contain nitrogen (providing that they are even-electron ions). The only reasonable structures compatible with these results were respective *p*-halophenolate anions. The structure of these ions, taking as an example the reaction product between 5-chloro-2-nitrophenide anion with acetonitrile, was proven by comparison of the appropriate CID spectra. It has to noted, however, that this proof is not conclusive because CID spectra of all three isomeric chlorophenolate anions are very similar under identical collision energy.

The formation of *p*-halophenolate anions can be rationalized by the mechanism shown in Scheme 6. Moving backwards from the final product, its formation can be rationalized by the well-known nitro to nitrito group rearrangement of the *p*-halonitrobenzene radical anion followed by the elimination of NO˙ [29, 30]. At the present stage of investigation, we can propose two possible pathways leading to this intermediate. Both paths start with the formation of the proton-bound complex between the nitroarene anion and C–H acid. This complex can undergo further transformation in two ways: (1) by heterolytic cleavage of the H–R bond giving *p*-halonitrobenzene-R$^-$ ion-molecule complex followed by the single electron-transfer (SET) process from R$^-$ to halonitroarene or (2) by homolytic cleavage of the H–R bond yielding directly *p*-halonitrobenzene radical anion and radical R[52.]

The participation of the single electron-transfer step
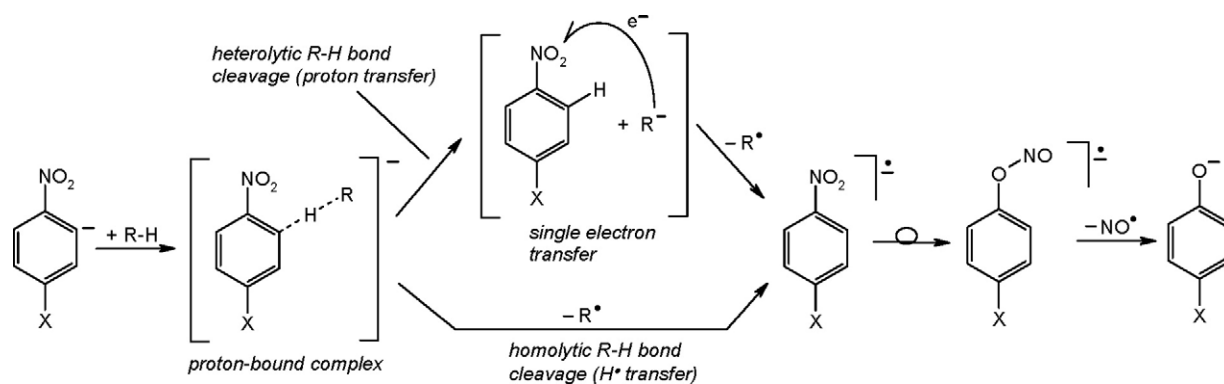
Scheme 6. Proposed mechanisms of the formation of *p*-halophenolate anions (X = F, Cl).
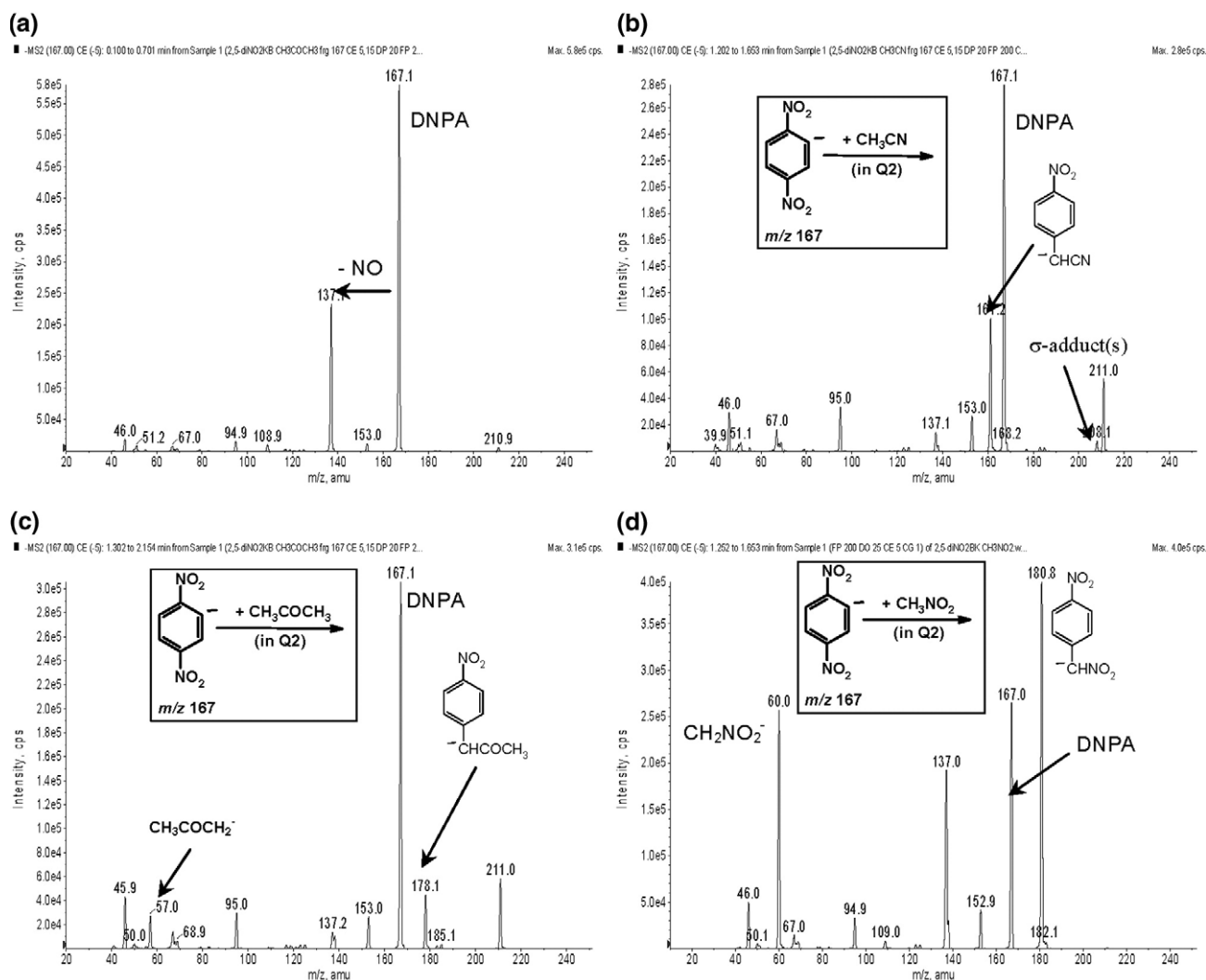
Figure 5. Q3 mass spectra recorded for 2,5-dinitrophenide anion selected with Q1: (**a**) no reagent added to the collision gas, (**b**) acetonitrile added to the collision gas, (**c**) acetone added to the collision gas, and (**d**) nitromethane added to the collision gas. Collision energy was set to 5 eV in all cases. DNPA = 2,5-dinitrophenide anion. M/z 211 peak corresponds to 2,5-dinitrobenzoate anion which is formed be a very efficient reaction of dinitrophenide anion with CO_2 present in a trace amounts in a collision gas.

in the aromatic nucleophilic substitution reactions and related processes is an old and intensively discussed problem [31–33]. In principle, one can imagine that the formation of the σ-adduct can proceed not only in a direct reaction between the nitroarene and the carbanion but also in a two-step process: (1) single electron-transfer from the carbanion to the nitroarene and (2) recombination of the nitroarene radical anion with the radical formed from the carbanion. Our results show that the SET mechanism can be applied also for rationalization of the gas-phase reactions. The question appears, however, if such processes are possible thermochemically. Simple estimations using the respective proton and electron affinities data show that this reaction can proceed. For example, the enthalpy of the transformation of 5-chloro-2-nitrophenide anion and

acetonitrile into p-chloronitrobenzene radical anion and $\cdot CH_2CN$ radical is about 6.4 kcal/mol. Similar results were obtained for the reaction with acetone (8.2 kcal/mol). Taking into account that the formation of the anion-molecule complex in the gas phase is exothermic by about 10 to 20 kcal/mol [8, 9], there is enough energy left to facilitate the reaction. The internal energy of the ion-molecule complex is even higher due to the collision energy (E_{lab} = 5 eV which for the reaction of 5-chloro-2-nitrophenide anion with acetonitrile corresponds to E_{CM} = 1.04 eV $\cong$ 24 kcal/mol). We have proven also that the increase of the collision energy from 5 to 15 eV (laboratory frame) increases the intensity of m/z 127 peak, corresponding to the p-chlorophenolate anion, very significantly. For the reaction mentioned above, it becomes basic peak in the spec-

trum. We found that the formation of halophenolate anions is characteristic, to more or less extent, for all reactions studied within this work but more detailed discussion of this subject is outside the scope of this paper. There is no doubt that this interesting reaction requires further investigations, including advanced molecular modeling.

In solution chemistry, not only halogen atoms but also NO$_2$ group is a good leaving group in S$_N$Ar reactions. Following this observation, we performed a series of experiments with 2,5-dinitrophenide anion (formed from the 2,5-dinitrobenzoate anion) and a number of C–H acids. The results are presented in Figure 5. All three C–H acids, acetonitrile, acetone, and nitromethane gave ions corresponding to the expected S$_N$Ar reaction products. However, in the case of acetonitrile and acetone, the reaction efficiency was quite low, especially when compared with the reactions of halonitrophenide anions. These results can be rationalized by much lower proton affinity of 2,5-dinitrophenide anion compared with its halonitro analogues (Table 1). Consequently, the proton transfer reactions are endothermic in this case, which results in their lower efficiency. On the other hand, endothermicity of the proton transfer step should stabilize the resulting σ-adduct, which is not observed; only in the spectrum of the reaction products with acetonitrile relatively small peak corresponding to the σ-adduct can be seen. The only reasonable explanation for this fact is the very high reactivity of the σ-adducts formed with *p*-dinitrobenzene towards S$_N$Ar or other reactions products.

Much higher efficiency shows the reaction with nitromethane, which is significantly more acidic than acetonitrile and acetone. In this case, the proton transfer reaction is exothermic by about 7 kcal/mol, which facilitates the substitution reaction. The results of this reaction we were able to compare with those described by Cooks et al. in 2004 [21]. In their work, these authors studied, among others, the gas-phase reactions of *o*-, *m*-, and *p*-dinitrobenzene with nitromethyl anion generated in a CI source. In all three cases they were able to record *m/z* 228 anion corresponding to the respective σ-adducts. In the CID spectra of these anions obtained from *o*- and *p*-dinitrobenzenes (not from the *meta* isomer!) they observed *m/z* 181 ions for which they presented the following rationalization: ". . .the most likely structure of the fragment ion of *m/z* 181 is the phenide anion, formed through elimination of a hydrogen atom and nitro group, the product being resonance stabilized by an ortho or para nitro group." In our opinion, this structure is incorrect and, actually, they observed the S$_N$Ar reaction of the nitro group with nitromethyl anion. Reaction mechanisms proposed by Cooks et al. and by us are presented in Scheme 7.

To confirm our mechanism we compared CID spectrum of the *m/z* 181 ion resulting from the reaction of the 2,5-dinitrophenide anion (obtained by decarboxylation of 2,5-dinitrobenzoate anion) with nitromethane
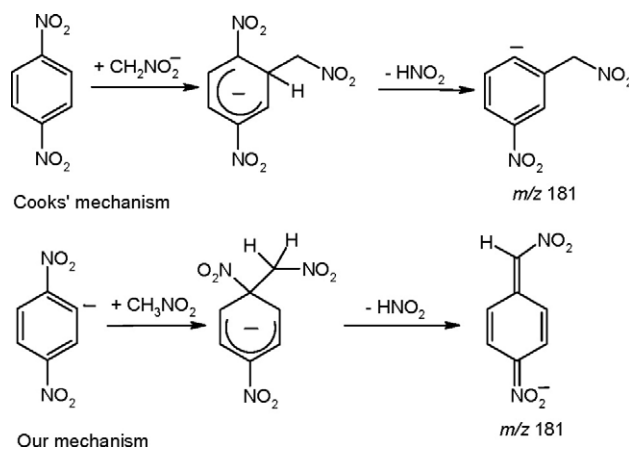
Scheme 7. Reaction mechanisms leading to the formation of the *m/z* 181 ion proposed by Cooks et al. [21] and by us.

in the ion source with CID spectra of the anions of model *o*-, *m*-, and *p*-nitrophenyl-nitromethanes (Figure 6). The result unequivocally shows that in the reaction described above (*p*-nitrophenyl)-nitromethyl anion is formed—not *meta* isomer proposed by Cooks. It has to be noted also that 4-nitro-2-nitromethyl-phenide anion proposed by Cooks (Scheme 7, upper part) should undergo very rapid 1,3-hydrogen shift from much more acidic -CH$_2$NO$_2$ group to the benzene ring. This process should lead to the much more stable (*m*-nitrophenyl)-nitromethyl anion. As we proved in our experiments, this was not the case.

It is interesting that Cooks et al. were able to observe the ions corresponding to the σ-adducts of nitromethyl anion also with *o*- and *p*-dinitrobenzenes. In our experiments, only *m*-dinitrobenzene gave stable σ-adduct. This is most likely the result of the different conditions in which σ-adducts were generated. Cooks used CI source in which ions reach thermal equilibrium. In our experiments, σ-adduct was formed in the reaction taking place within the ion-molecule complex formed as the result of a collision. Such ion cannot lose an excess of energy in a way other than fragmentation.

Conclusions

It was found that in the reactions of halonitro- and dinitrophenide anions with X (X = F, Cl, Br, NO$_2$) and NO$_2$ groups in *ortho* or *para* position to each other with selected C–H acids: CH$_3$CN, CH$_3$COCH$_3$, and CH$_3$NO$_2$, the S$_N$Ar-type reaction products are formed. In the case of F, Cl, and NO$_2$ derivatives the main ionic product is the respective [NO$_2$-Ph-CHR]$^-$ anion (R depends on the C-H acid used in the reaction, e.g., CN, COCH$_3$ and NO$_2$). In the case of Br derivatives the main ionic product is Br$^-$ ion because it has lower proton affinity that the [NO$_2$-Ph-CHR]$^-$ anion (for R = CN, COCH$_3$). For some halonitrophenide anion –C–H acid pairs of reactants the S$_N$Ar reaction is competed by the formation of halophenolate anions. This reaction can be
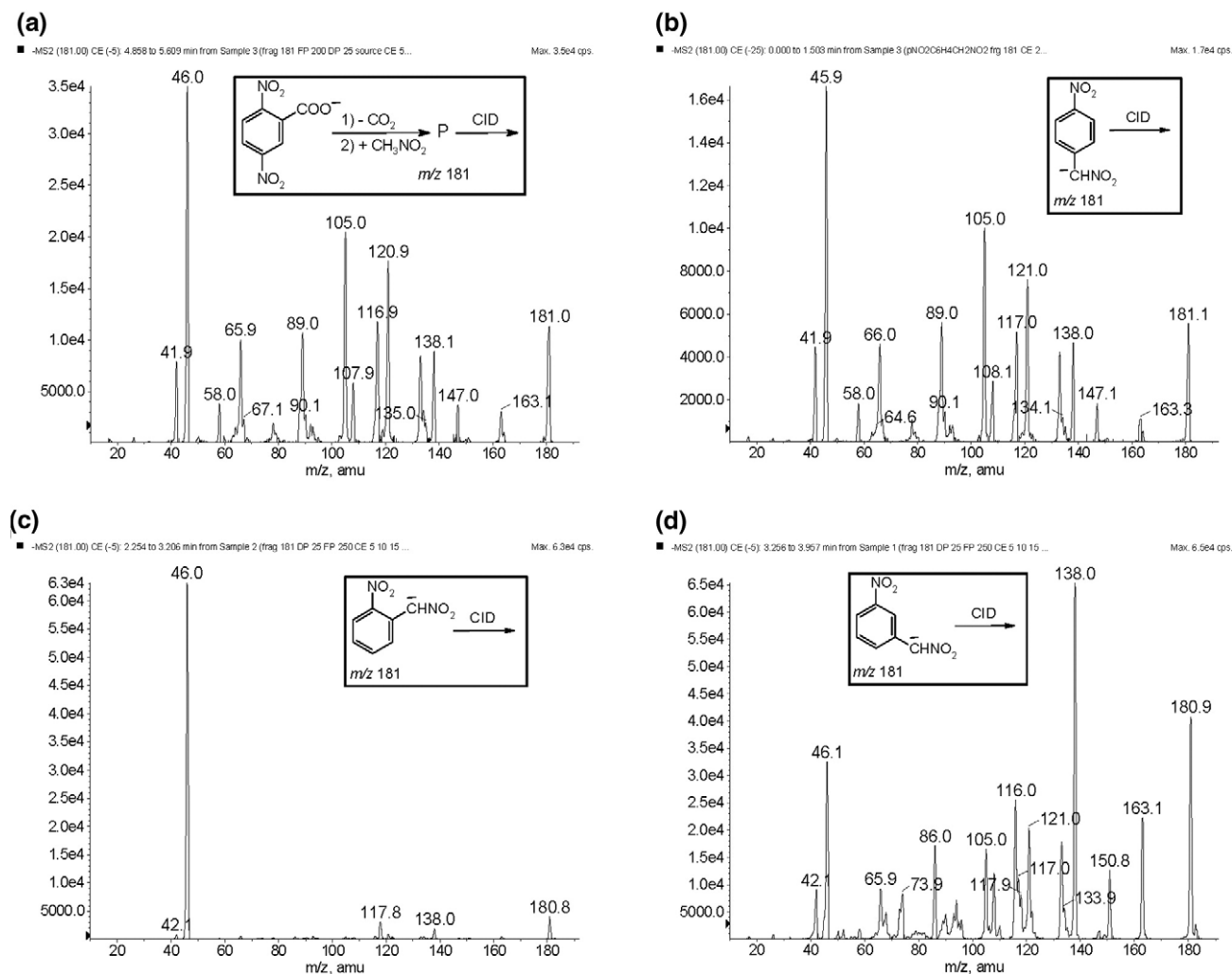
Figure 6. CID spectra recorded with the same collision energy for: (**a**) *m/z* 181 ion resulting from the reaction of the 2,5-dinitrophenide anion with nitromethane in the medium-pressure zone of the ESI ion source; (**b**), (**c**), and (**d**) [M − H]⁻ ion generated, respectively, from the *p*-, *o*-, and *m*-nitrophenylnitromethane in the ESI ion source under standard conditions.

rationalized by the single electron-transfer or hydrogen atom transfer mechanisms.

Our results show that the S_NAr-type reactions of the *ortho* and *para* isomers of halonitro- and dinitroarenes are easy to perform in the gas phase, and can be used for studying these processes in the solvent-free environment or, following the route introduced by Cooks and coworkers, can be used for analytical purposes.

Addendum

After this paper had already been submitted for publication, an article appeared in which the authors proved by IR spectra the presence of the σ-adduct between 1,3,5-trinitrobenzene (TNB) and methoxide anion in the gas phase [34]. They also showed, using advanced DFT calculations, that the σ-adduct is the most stable structure compared with ion-molecule complexes formed by TNB anion and methanol.

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