

Gas-phase interaction between nickel (II) and nitrobenzyl azides: An ESI-MSⁿ study

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ABSTRACT

Organoazides are intermediates in the synthesis of imidometal complexes. Metalimido complexes have an important role in catalysis. Thus, the organoazide interaction with metals is an important issue. However, the isolation of organoazidometal complexes is difficult due to the easy loss of N₂.

The present study describes the complexation of nickel by nitrobenzyl azides by means of electrospray ionization mass spectrometry (ESI-MS), which was used also as a probe for the characterization of isomers. Organoazidometal complexes were observed and isolated from solutions of NiCl₂ and NiBr₂ in methanol/water. A different solvent, ethanol/water was also used. The complexes detected were singly and doubly positively charged, with various stoichiometries. The most abundant species were [Ni(II)Az₃]²⁺ for *ortho*- and *para*-isomers, and [Ni(II)Az₃(H₂O)]²⁺ for meta isomer, where Az stands for nitrobenzyl azides. The *ortho* isomer showed several single positively charged complexes integrating chloride as a ligand. The mass spectra of the three isomers allowed their differentiation based on different behaviour in the mass range *m/z* 296–*m/z* 312. The MS² spectra of [Ni(II)Az₃]²⁺ were investigated aiming to characterize the three isomers but this analysis was not absolutely conclusive about the coordination site(s). Density functional theory calculations provided possible structures for the [Ni(II)Az₃]²⁺ cation with the different isomers and their coordination modes could be responsible for their fragmentation pathways.

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1. Introduction

Industrial interest in organic azides arises from the use of these compounds in the synthesis of heterocycles and complex structures in biochemical applications, as a functional group in pharmaceuticals [1–3], as inhibitors of cysteine proteases and cyclooxygenase-2 [4,5]. In particular, the aromatic azide moiety has been applied as starting material in organic synthesis [6–10] and nitrobenzyl azides have been reported as starting material for the synthesis of

biologically active compounds [11,12] and also for the modification of polymer surfaces [13].

Some of the applications involve the interaction of organic azides with metals. For example, in materials science, azides are used in the preparation of nano-sized materials and thin films by deposition of nitride layers on metal surfaces [14,15]. In organic synthesis, the interaction of azides with metals is exemplified by the Cu(I)-catalyzed azide-alkyne cycloaddition [16–18], as well as with ruthenium [19,20]. Organoazido metal complexes have been explored as intermediates in the synthesis of imido metal complexes. Imido metal complexes have received increased interest due to their reactivity, particularly, in catalysis, nitrogen fixation and atom-/group-transfer processes [21–27]. Nevertheless, the isolation and characterization of organoazido metal complexes is difficult due to the rapid loss of nitrogen [21–25,27]. Furthermore, the azido group is able to coordinate through the terminal nitrogen atom (N_γ) or the alkylated nitrogen atom (N_α) [21–25,27]. Given the above mentioned importance of the reactivity of organoazides towards metal ions, we decided to study their interactions by

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means of mass spectrometry techniques. Up to now, our research has been focused on the study of the interaction of aliphatic azides (azidoacetone and 3-azidopropionitrile) with nickel, cobalt, calcium and magnesium [28–30]. The chosen aliphatic azides had two functional groups in order to investigate the possibility of a chelation effect as observed in the Barz et al. study [24]. In our previous studies coordination by N γ nitrogen or by the alkylated N α nitrogen as well as chelation were detected in some situations [30]. Moreover, when the organic azides interacted with transition metals, a C–C bond activation and metal insertion were detected [28,30].

Most of the reported studies on imidometal complex synthesis have involved phenyl, benzyl, and mesityl azides where aromatic ring did not participate in the coordination [21–25,27,31]. In some cases, structural data for the unstable intermediates, the organoazidemetal complexes, were obtained by means of X-ray studies. To the best of our knowledge there are no reports in the literature on the application of electrospray mass spectrometry (ESI-MS) to study these interactions and isolate and characterize intermediates.

Thus, the present study investigates the interaction of bifunctional organoazides, possessing an aromatic ring (nitrobenzylazides) with nickel. The choice of transition metals was not fortuitous since, for example, nickel is a relevant metal in both biological [32] and catalytic processes [33].

Electrospray ionization (ESI) mass spectrometry combined with theoretical calculations should provide a good alternative to obtain structural information on the labile organoazide metal complexes. ESI is a soft ionization technique, and has been shown to be able to transfer solvated ions from solution to the gas phase while preserving non covalent interactions [34,35]. Therefore, ESI mass spectrometry has been particularly suitable to study metal ions complexed by organic ligands in the gas phase [36–38]. Moreover, it has been reported that combining metal interactions and tandem mass (MS/MS) may lead to an unequivocal identification of isomers [39–41]. Consequently, the distinction of the three nitrobenzyl azide isomers was attempted on the basis of the analysis of the full scan ESI mass spectra of metal–azide solutions and also by means of tandem mass spectrometry and collision induced dissociations (CID) of a few complexes identified. Density functional theory (DFT) calculations were also performed to aid the interpretation of the experimental data and to assign ion structures.

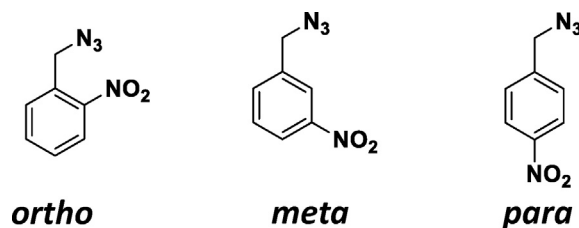
2. Experimental

2.1. Synthesis of nitrobenzyl azide isomers

Sodium azide (2 equiv.) was added slowly to a solution of the appropriate nitrobenzyl halide in dimethyl sulfoxide [42]. The mixture was stirred at room temperature protected from light until TLC analysis (hexane:dichlorometane 7:3) indicated completion of the reaction. Afterwards, the mixture was quenched with distilled water and extracted with diethyl ether. The combined organic phases were dried over anhydrous sodium sulphate, filtered and concentrated. After preparative TLC, the obtained product ($\eta > 90\%$) was analysed by FTIR (Mattson Satellite-FTIR) and by NMR (Brüker ARX400) spectroscopy.

2-Nitrobenzyl azide: IR data (neat): ν_{\max} 2105 (N $_3$) cm^{-1} ; ^1H NMR data (400 MHz, CDCl_3): δ 4.85 (s, CH $_2$), 7.50–7.54 (m, CH arom.), 7.66–7.71 (m, CH arom.), 8.11–13 (m, CH arom.) ppm; ^{13}C NMR data (100 MHz, CDCl_3): δ 51.9 (CH $_2$), 125.2, 128.9, 130.1, 131.5, 133.9, 147.7 ppm.

3-Nitrobenzyl azide: IR data (neat): ν_{\max} 2104 (N $_3$) cm^{-1} ; ^1H NMR data (400 MHz, CDCl_3): δ 4.50 (s, CH $_2$), 7.55–7.67 (m, CH arom.), 8.18–8.20 (m, CH arom.) ppm; ^{13}C NMR data (100 MHz, CDCl_3): δ 53.7 (CH $_2$), 122.8, 123.1, 129.8, 133.8, 137.6, 148.5 ppm.



Scheme 1. Structure of the nitrobenzyl azides under study.

4-nitrobenzyl azide: IR data (neat): ν_{\max} 2106 (N $_3$) cm^{-1} ; ^1H NMR data (400 MHz, CDCl_3): δ 4.52 (s, CH $_2$), 7.51 (d, J 8.4 Hz, CH arom.), 8.25 (d, J 8.8 Hz, CH arom.) ppm; ^{13}C NMR data (100 MHz, CDCl_3): δ 53.6 (CH $_2$), 123.9, 128.5, 142.7, 147.6 ppm.

The structures of the nitrobenzyl azides under study are presented in Scheme 1.

2.2. Mass spectrometry

In order to avoid the decomposition of *ortho*-, *meta*- and *para*-nitrobenzyl azides, they were stored in dry ice and when used in experiments, the sample was maintained at room temperature and shielded from light to prevent photolysis.

The metallic salts used in this study, without further purification, were: nickel chloride (Aldrich 98%) and nickel bromide (Merck > 98%). Methanol and ethanol (Merck, 99.9%) HPLC grade, and water doubly distilled were used as solvents.

Solutions, 5 mmol L $^{-1}$ of nickel chloride and nickel bromide were prepared in a 1:1 water/methanol (v/v) solvent mixture as well as in a water/ethanol solvent mixture (v/v). Nitrobenzyl azides were added to the salt solutions, to a final concentration of 65 mmol L $^{-1}$ in nitrobenzyl azides.

All experiments were performed using a LCQ Duo ion trap mass spectrometer from Thermo Finnigan (San Jose, CA, USA) equipped with an electrospray ion source. Samples were introduced, via a syringe pump (flow rate of 5 $\mu\text{L min}^{-1}$), into the stainless steel capillary of the electrospray ion source. The applied spray voltage in the source was 4.5 kV, the capillary voltage was 7–10 V and the capillary temperature was 200–220 $^{\circ}\text{C}$. All the other mass spectrometer parameters were also adjusted, in order to optimize the signal-to-noise ratios for the ions of interest. Nitrogen was used as the nebulizing and drying gas in the source.

The measured pressure during experiments at the skimmer cone with a convectron gauge was normally 1.33×10^2 Pa. The base pressure in the ion trap housing with helium added was typically 1.49×10^{-3} Pa.

The data were acquired in the positive ion mode. The MS full scan spectra were recorded in the range m/z 50–500 (since no ions were detected above m/z 500) and three micro-scans were averaged. Collision induced dissociation (CID) and MS n ($n \geq 2$) experiments were performed with helium, at various normalized collision energy (NCE) values given in percentage. The range from 0% to 100% corresponds to a resonant excitation AC signal of 0–2.5 V (zero-to-peak) at the secular frequency of the precursor ion [43]. The NCE was gradually increased until the precursor and the product ions could, both, be observed in the MS 2 spectrum. Injection times were 50 ms in a full scan and 200 ms in a MS/MS scan. XcaliburTM software was used to acquire and process the data.

High-resolution mass measurements were performed on an Apex Ultra FTICR mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with an Apollo II dual ESI/MALDI source (Bruker Daltonics, Bremen, Germany). The analyte solutions were infused into the mass spectrometer at a flow rate of 120 $\mu\text{L h}^{-1}$ by means of an infusion pump (KD Scientific, Holliston, MA, USA). The

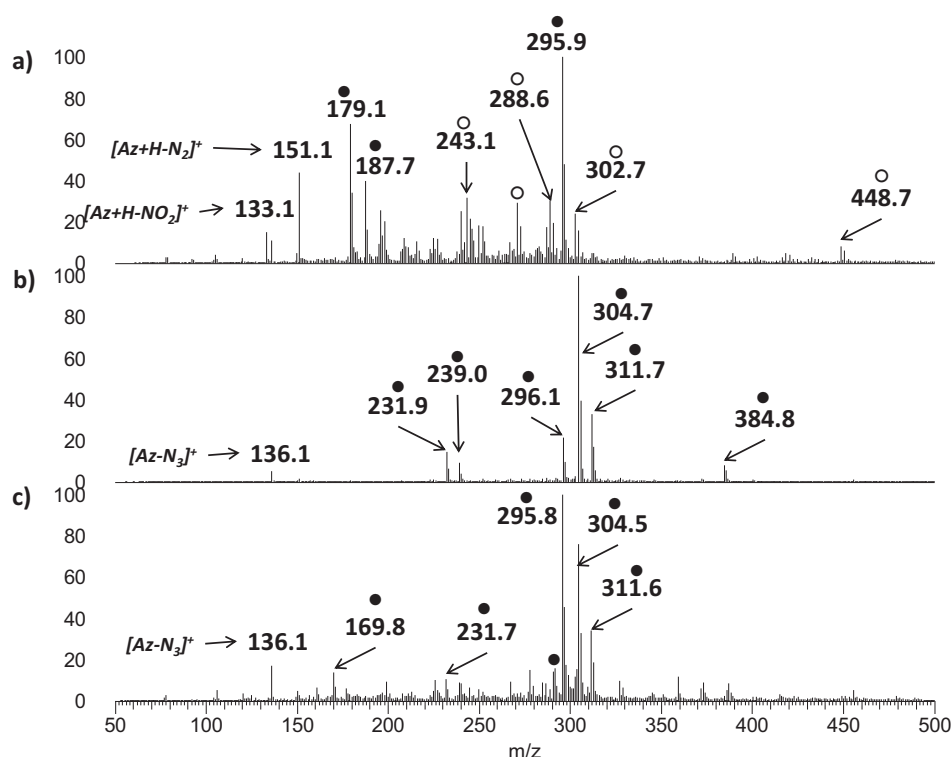


Fig. 1. Mass spectra of: (a) *ortho*-; (b) *meta*- and (c) *para*-nitrobenzyl azides and NiCl_2 in 50/50 (v/v) $\text{CH}_3\text{OH}/\text{H}_2\text{O}$. (● – doubly charged ions; ○ – singly charged ions).

mass spectra presented are the average of 32 scans. The ions were accumulated in the collision cell for 0.5 s prior to their transfer to the ICR cell.

2.3. Theoretical calculations

The DFT calculations were performed with Gaussian03 [44] using the hybrid B3LYP functional [45,46]. The standard 6–31 + G* basis set was used for all elements except nickel which was described by the LanL2DZ basis set with the associated ECP [47–50] augmented by an f polarization function (exponent 3.130) [51]. All geometry optimizations were performed without symmetry constraints and frequency calculations were performed to check the nature of the stationary points.

3. Results and discussion

3.1. Mass spectrometry

The present work extends the previous investigation on the complexation of metals with aliphatic azides as ligand [28–30], by studying the complexation of nickel with azides attached to an aromatic ring, nitrobenzyl azides. The metal cation $\text{Ni}(\text{II})$ was generated in solution from chloride or bromide salts. The mass spectra of 50/50 (v/v) $\text{CH}_3\text{OH}/\text{H}_2\text{O}$ solutions of NiCl_2 and each nitrobenzyl azide isomers are presented in Fig. 1.

The ions observed in these solutions are summarized in Table 1, which contains the complex ion composition, the monoisotopic m/z values and their relative abundances observed in the MS spectra for the studied isomers. The first step for the assignments was to consider the combination of the mass and the overall charge of a given ion, the isotopic pattern of its envelope and the ion monoisotopic mass. Ions at m/z 133, 136 and 151 that appear in the ESI mass spectra of the solutions of nitrobenzyl azides and NiCl_2 (Fig. 1) were

attributed to nitrobenzyl azide fragmentation [52] and not to metal complexes, as such, they are not included in Table 1 nor in Schemes.

Nitrobenzyl azides and $\text{Ni}(\text{II})$ established complexes having different stoichiometries and different charged states (Fig. 1 and Table 1). *Ortho*-nitrobenzyl azide presented singly and doubly charged ions. Most of them were singly charged due to the presence of Cl^- as ligand. *Meta*-nitrobenzyl azide only presented doubly charged ions. For *para*-nitrobenzyl azide, complex ions were mainly doubly charged as for the *meta*-isomer.

The charge state was inferred from the MS spectra where, for example, doubly charged ions were identified by the half m/z value of each peak. In addition, the peaks within the isotopic envelope were displayed at half of their mass difference. Furthermore, in the MS/MS analysis, losses of certain ligands were detected at half masses. The confirmation of the assignments relied, mainly, on isotopic patterns and the MS^2 spectra. Other routes for confirmation were the m/z ratio displacement in a different solvent and/or with a different nickel salt, when a solvent molecule and/or an anion of the salts were suspected of behaving as ligands.

Among the three isomers, *ortho*-nitrobenzyl azide was particularly suitable for the exchange of salt study, since it shows the largest number of singly charged ions due to the presence of chloride ligand. When nickel chloride was substituted by nickel bromide, the complexes assigned as containing one chloride ligand were displaced by 44 Da, as it can be seen in Table 2. The *para*-isomer also showed the displacement of some of the m/z values. For example, the ions at m/z 289 and 303 (NiCl_2 system) were displaced to m/z 333 and 347, respectively, in the NiBr_2 system. Nevertheless, these ions had very low abundances which did not allow for a confirmation by isotopic pattern analysis. Furthermore, this study allowed the confirmation of the composition of the complexes that did not contain halogens. For these complexes the m/z displacement did not occur (Table 2).

Some of the complexes seemed to be solvated with methanol or water. These assignments were confirmed by changing the

Table 1
Assignment of complexes formed from 50/50 (v/v) CH₃OH/H₂O solution of nickel(II) chloride in the presence of nitrobenzyl azides.

Complex ion composition	<i>m/z</i>	<i>Ortho</i> Rel. ab. (%)	<i>Meta</i> Rel. ab. (%)	<i>Para</i> Rel. ab. (%)
[Ni(II)Az ₂ Cl] ⁺	449	8	–	–
[Ni(II)Az ₄] ²⁺	385	–	8	–
[Ni(II)Az ₃ (CH ₃ OH)] ²⁺	312	5	33 ^a	34 ^a
[Ni(II)Az ₃ (H ₂ O)] ²⁺	305	–	100	77 ^b
[Ni(II)AzCl(CH ₃ OH)] ⁺	303	37 ^a	–	15
[Ni(II)Az ₃] ²⁺	296	100	22	100
[Ni(II)Az(Az-NO)(Az-NO ₂)(H ₂ O) ₂ (CH ₃ OH)] ²⁺	292	–	–	16
[Ni(II)Az ₂ (Az-N ₂)(H ₂ O)] ²⁺	291	–	–	14
[Ni(II)AzCl(H ₂ O)] ⁺	289	30	–	5
[Ni(II)Az(N ₃)] ⁺	278	5	–	15
[Ni(II)AzCl] ⁺	271	29	–	–
[Ni(II)(Az-N ₂)(Az-NO) ₂] ²⁺	252	18	–	–
[Ni(II)(Az-N ₂)Cl] ⁺	243	31	–	–
[Ni(II)Az ₂ (CH ₃ OH) ₂] ²⁺	239	–	9 ^a	9 ^a
[Ni(II)Az ₂ (H ₂ O)(CH ₃ OH)] ²⁺	232	–	15 ^a	10 ^a
[Ni(II) ₂ (Az-N ₂)Cl ₂ (H ₂ O) ₃] ²⁺	195	10	–	–
[Ni(II)(Az-N ₂) ₂ (H ₂ O)] ²⁺	188	40	–	–
[Ni(II)(Az-N ₂) ₂] ²⁺	179	68	–	–
[Ni(II)(Az-N ₂ -HCN) ₂ (H ₂ O) ₂] ²⁺	170	–	–	14
[Ni(II)(Az-N ₂ -HCN) ₂ (H ₂ O)] ²⁺	161	–	–	6

^a The assignment was confirmed by solvent substitution experiments (see text).
^b Include the isotopic contribution of ion at *m/z* 303.

solvent system from methanol/water to ethanol/water. Besides confirming the presence of solvent molecules, this study also provided information about the charge of the complex. For doubly charged complexes the *m/z* displacement, due to the exchange of methanol by ethanol, is 7 Da while for singly charged species the displacement is 14 Da. This procedure allowed us to confirm that the *ortho*- and *meta*-isomers showed three complexes incorporating methanol molecules while the *para*-isomer formed six.

For all three isomers, the ions at *m/z* values lower than 296 were assigned to complexes bearing fragmented azide ligands. These encompassed losses of N₂, a very common loss in organic azides [1–3,21,22,28,30], and losses of NO₂, NO and N₃, which were also detected in a previous nitrobenzyl azide study [52]. The most striking example of these low *m/z* ions was at *m/z* 179 for the *ortho*-isomer, which is characteristic of this isomer and was attributed to [Ni(II)(Az-N₂)₂]²⁺. This attribution was confirmed by MS² experiments (see Supplementary Information, Fig. S1) and also by accurate mass measurements (*m/z* deviation < 0.5 ppm).

After applying the identification strategies discussed so far, the ESI mass spectra of the solutions bearing each of the three isomers and Ni(II) ions were analysed. The base peak for the *ortho*- and *para*-isomer was at *m/z* 296, attributed to [Ni(II)Az₃]²⁺, while for the *meta*-isomer the base peak was at *m/z* 305, attributed

Table 2
Assignment of nickel complexes with *ortho*-nitrobenzyl azide from NiCl₂ and NiBr₂ solutions in H₂O/CH₃OH.

Complex ion composition	X=Cl		X=Br	
	<i>m/z</i>	Rel. ab. (%)	<i>m/z</i>	Rel. ab. (%)
[Ni(II)Az ₂ X] ⁺	449	8	493	6
[Ni(II)Az ₃ (CH ₃ OH)] ²⁺	312	5	312	24
[Ni(II)AzX(CH ₃ OH)] ⁺	303	37	347	11
[Ni(II)Az ₃] ²⁺	296	100	296	100
[Ni(II)AzX(H ₂ O)] ⁺	289	30	333	11
[Ni(II)AzX] ⁺	271	29	315	41
[Ni(II)Az(Az-N ₂) ₂] ²⁺	268	6	268	57
[Ni(II)(Az-N ₂)(Az-NO) ₂] ²⁺	252	18	252	8
[Ni(II)(Az-N ₂)X] ⁺	243	31	287	50
[Ni(I)(Az-N ₂)(CH ₃ OH)] ⁺	240	25	240	13
[Ni(II) ₂ (Az-N ₂)Cl ₂ (H ₂ O) ₃] ⁺	195	10	239	12
[Ni(II)(Az-N ₂) ₂ (H ₂ O)] ²⁺	188	40	188	–
[Ni(II)(Az-N ₂) ₂] ²⁺	179	68	179	8

to [Ni(II)Az₃(H₂O)]²⁺. These two ions differ only by one water molecule and provided tool to distinguish *meta*- from *ortho*- and *para*-isomers. The formation of abundant species with three ligands was also observed for azidoacetone [30] and 3-azidopropionitrile [28]. In the present case the three ligands were azides, whereas for the other compounds the ligands were two azides and one halogen.

The *ortho*-isomer coordinates to the metal centre (nickel) and, frequently, chloride ion is also coordinated. This behaviour resulted in the formation of several singly charged ions with a relatively high abundance (e.g. *m/z* 303, 289, 271 and 243). The abundance of the *m/z* 449 ion was only ca. 8%, however this species only formed with the *ortho*-isomer and it can be considered as a diagnostic ion and was attributed to [Ni(II)Az₃Cl]⁺ by accurate mass measurements (mass deviation < 1 ppm) and also by MS² experiments (see Supplementary Information, Fig. S2).

The *meta*-isomer presented fewer complexes, all of them were doubly charged, and, with the exception of the ion at *m/z* 296 attributed to [NiAz₃]²⁺, the remainder of the complexes incorporated solvent molecules as ligands.

The behaviour of the *para*-isomer was a mixture of the other two. The base peak was at *m/z* 296, as it was observed for the *ortho*-isomer. Complexes bearing chloride as ligand were detected for the *para*-isomer, however, these were not as abundant as for the *ortho*-case. On the other hand, the *para*-isomer showed some complexes that were detected for the *meta*- (e.g. *m/z* 312, 305, 239 and 232) which were absent in *ortho*-.

Therefore, the three isomers were distinguishable by their full scan mass spectra. This is quite clear in Fig. 1 which shows that *m/z* 290–320 interval was crucial to characterize and partially differentiate these isomers. Furthermore, ions at *m/z* 179 and 449 were characteristic of the *ortho*- isomer serving as diagnostic ions.

MS² and CID experiments were performed on the majority of the ions detected in the ESI mass spectra of these isomers; nevertheless one result is worth mentioning in more detail. As stated earlier in this discussion, the ion at *m/z* 296 was a very important one for the three isomers. When the ion at *m/z* 296 was isolated in the ion trap and fragmented through collision induced dissociation a different behaviour was observed which will be discussed in the following section.

3.2. MS² experiments on the *m/z* 296 ion

The MS² spectra of the ion at *m/z* 296 are depicted in Fig. 2. It is quite clear that, although these ions have the same composition, their structures are certainly different as their MS² spectra, taken at the same NCE value, are quite different from each other. Furthermore, although the base peak in the full mass scan was the same for the nickel complexes coordinating the *ortho*- and *para*-nitrobenzyl azides, a careful comparison of the MS² spectra of all three isomers showed more similarities between fragmentation pathways for the *meta*- and *para*- than with the *ortho*- and *para*-nitrobenzyl azides. The *ortho*- counterpart did not show significant product ions above *m/z* 296. The only ions with significant abundance were at *m/z* 314, which can be attributed to a solvation product $[\text{Ni}(\text{II})\text{Az}_3(\text{H}_2\text{O})_2]^{2+}$, and at *m/z* 328, which can be attributed to $[\text{Ni}(\text{II})\text{Az}_3(\text{CH}_3\text{OH})_2]^{2+}$. Gas phase solvation is quite uncommon and is probably due to the occurrence of ion molecule reactions within the ion trap. Such behaviour is documented in the literature for ionic liquids [53] and for metal complexes [54–56] including metal–azide complexes [28,30]. Nevertheless, to the best of our knowledge two authors, Perera et al. [54] and Wickens et al. [56], propose a source for the neutral molecules in the ion trap. The origin of H₂O in the bath gas, in our case helium, can be easily understood since water is present in trace amounts in the helium. For the other solvent molecules this rationale may not be applied since they are not present as impurities. Perera et al. [54] proposed that solvent molecules may adsorb to the metal surfaces of the ion trap and also to the surrounding vacuum hardware and eventually constitute a fraction of the total bath gas pressure. However, Wickens et al. [56] found that the partial pressure of solvent vapour in the source is sufficient for transmission through the various pumping stages of the vacuum system to the analyser region of the instrument. Both hypotheses seem to be plausible, nevertheless further investigation on this subject is needed.

The main fragmentation channel for the *ortho*-nitrobenzyl azide complex at *m/z* 296 ($[\text{Ni}(\text{II})\text{Az}_3]^{2+}$), yielded an ion at *m/z* 230 which corresponded to a *m/z* loss of 66. Both of these ions were doubly charged, according to the MS² spectra of *m/z* 296 and 297 (see Supplementary Information, Fig. S3), thus, the real mass loss would be 132 Da. This is consistent with the release of C₆H₄CH₂N₃, the NO₂ group remaining coordinated to the metal centre. Thus, at least one of the azide moieties was coordinated to the metal centre by the NO₂ group. The ion at *m/z* 179 can be attributed to a product ion bearing Ni in its structure. In order to clarify this issue we decided to isolate the ⁶⁰Ni isotope of the ion at *m/z* 296 (i.e. *m/z* 297) and fragment it within the ion trap (see Supplementary Information, Fig. S3). Using this procedure, the *m/z* values of the ions bearing Ni within their structures would be displaced by one *m/z* unit (in the case of doubly charged ions) and two *m/z* units (for singly charged ions). In fact, for the ion at *m/z* 179 the behaviour of a doubly charged ion was found. Hence, the formation of the ion at *m/z* 179 can be attributed to a combined loss of one azide ligand (178 Da) and two N₂ (56 Da) resulting in $[\text{Ni}(\text{II})(\text{Az}-\text{N}_2)_2]^{2+}$. The proposed sequential fragmentation of the complex ion at *m/z* 296 for the *ortho*-isomer is presented in Scheme 2.

The *meta*- and *para*-isomers, besides being distinguishable by the full scan mass spectra, were also quite easily distinguishable by the MS² spectra of the ion at *m/z* 296. The first striking difference was the abundance of the ion at *m/z* 305, attributed to solvation of the precursor ion (*m/z* 296). This ion showed a higher abundance for the *meta*-isomer than for the *para*-, which was a first indication of a possible different ion structure for each isomer. There were two other differences that distinguish these isomers. One was the ion at *m/z* 428, formed only with the *meta*-isomer and the other was the ion at *m/z* 401, formed only for the *para*-isomer. The *m/z* 428

ion could be attributed to $[\text{Ni}(\text{II})\text{Az}(\text{Az}-\text{N}_2)\text{N}_3]^+$ and results from the combined loss of NO₂C₆H₄CH₂ (note that the N₃ group remains coordinated to the metal) and N₂. When the loss of NO₂C₆H₄CH₂ occurs, the azide group remained coordinated to the metal centre as a radical species or bearing a negative charge (N₃[−]). The latter behaviour is consistent with several reports in the literature where organic azides are similar to organic halogen compounds [2]. The ion at *m/z* 401, can be attributed to $[\text{Ni}(\text{II})\text{Az}(\text{Az}-\text{N}_2-\text{HCN})\text{N}_3]^+$ and resulted from a combined loss of NO₂C₆H₄CH₂, N₂ and HCN. Furthermore, the ion at *m/z* 136, detected in the MS² spectra depicted in Fig. 2b and c, can be attributed to NO₂C₆H₄CH₂⁺, a known product ion of the fragmentation of nitrobenzyl azides [52].

For the *meta*- and *para*-isomers, the most significant product ion, resulting from fragmentation of the ion at *m/z* 296, was at *m/z* 456. Taking into account the MS² spectra of ⁵⁸Ni and ⁶⁰Ni isotopes (see Supplementary Information, Fig. S3), the ion at *m/z* 456 was a singly charged one. This ion was formed through the loss of 136 Da from the doubly charged ion at *m/z* 296, which can be attributed to NO₂C₆H₄CH₂, the N₃ remaining coordinated to the metal centre, which implies that one of the azides is coordinated to the N₃ group. For the complex ions in which the N₃ remained coordinated, the charge may have resulted from a reduction of Ni(II) due to charge transfer after homolytic bond dissociation or from the presence of N₃[−], as mentioned above.

Scheme 3 shows a comparison of the sequential fragmentations of *m/z* 296 complex ion for *meta*- and *para*-isomers. Ions at *m/z* 305, 312 were water and methanol solvation products, respectively, of the precursor ion (*m/z* 296). The ion at *m/z* 428 was characteristic of the *meta*-isomer while the one at *m/z* 401 was characteristic of the *para*-isomer.

The ions at *m/z* 456, 428, 401, 250 in *meta*- and *para*-isomers allows us to conclude that one azide ligand may be coordinated by the azido group. The different fragmentation pathways obtained in the MS² mass spectra of *m/z* 296 were useful in order to characterize the three isomers. Nevertheless, they were not absolutely conclusive about the coordination sites. Thus, it was decided that some theoretical calculations would be necessary to obtain structural insights into the complexation of Ni(II) by nitrobenzyl azides.

3.3. Theoretical calculations

Given the different fragmentation pathways observed experimentally for the *m/z* 296, $[\text{Ni}(\text{II})\text{Az}_3]^{2+}$ ion, and the difficulty of establishing a single structure for this cation owing to the different coordination modes available, DFT calculations were performed for the nickel complexes coordinated to three ligands of the *ortho*-, *meta*-, and *para*-nitrobenzyl azides to try to relate their structural parameters with the observed fragmentation patterns.

The first difficulty arose from the fact that the Az ligand has some degree of conformational flexibility and is able to coordinate to the metal by both the −N₃ or the −NO₂ group. Therefore, several possible conformations and coordination modes were optimized for each isomer (*ortho*-, *meta*- and *para*-). All the resulting conformations are shown in the Supplementary Information (Figs. S4–S6) for *ortho*-, *meta*-, and *para*-, respectively while Fig. 3 depicts low-energy structures.

We began by analysing the $[\text{Ni}(\text{II})\text{Az}_3]^{2+}$ ion with the *ortho*-nitrobenzyl azide ligand. Their optimized lowest energy conformations are shown in Fig. 3 with their relative energies (kJ mol^{−1}).

The lowest energy conformation is **o.H** with one Az ligand coordinated by both oxygen atoms of the −NO₂ group (Ni–O distances of 1.937 and 1.969 Å). The remaining two Az ligands are coordinated by their −N₃ groups through the terminal N_γ nitrogen (Ni–N distances of 1.940 and 1.932 Å). Terminal coordination modes were

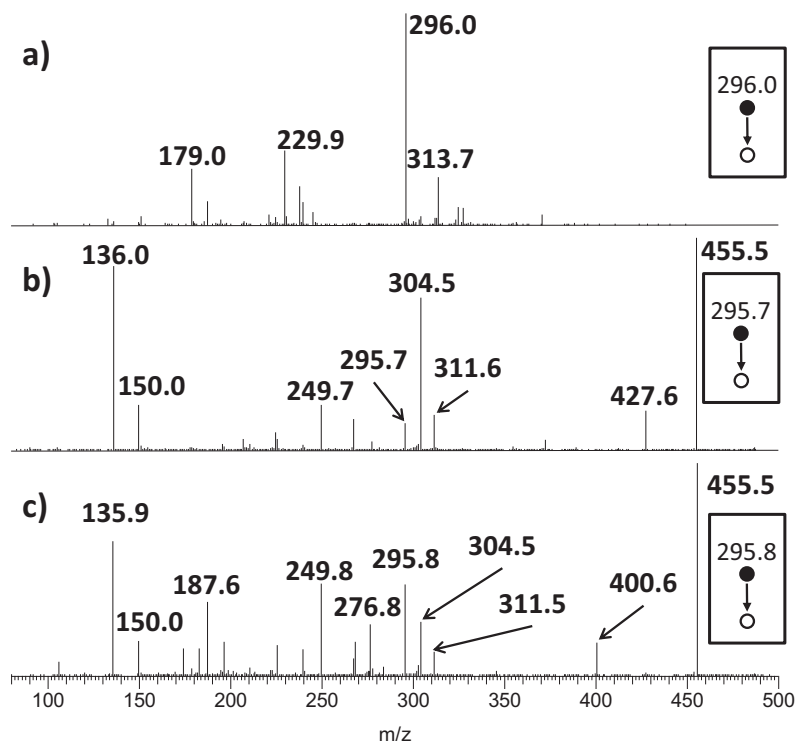
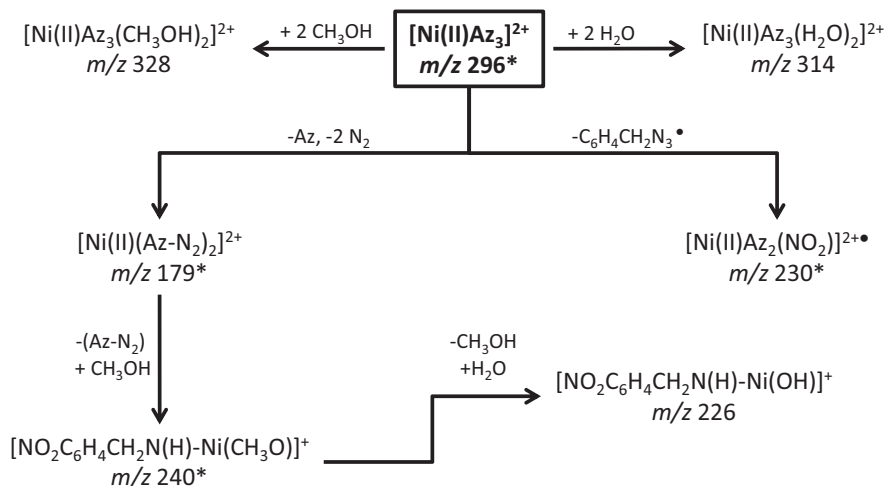


Fig. 2. MS² spectra of the ion at m/z 296 ion for: (a) *ortho*-; (b) *meta*- and (c) *para*-isomers. (collision energy was kept constant for all spectra, NCE = 15%).

also obtained in a previous study with Az=3-azidopropionitrile [57].

Remarkably, the “dangling” $-\text{NO}_2$ groups appear to establish a contact with nickel through the empty axial coordination positions. Although the Ni–O distances (2.748 and 2.725 Å) can be considered long for typical coordination, undoubtedly there is an interaction which appears to stabilize this coordination mode; indeed, when one of these interactions is removed in **o.G**, the energy increases to 20.2 kJ mol^{−1} (see Supplementary Information, Fig. S4). The *ortho*-position of the substituents enables this **o.H** conformation (see below for the *meta*- and *para*-isomers). Other

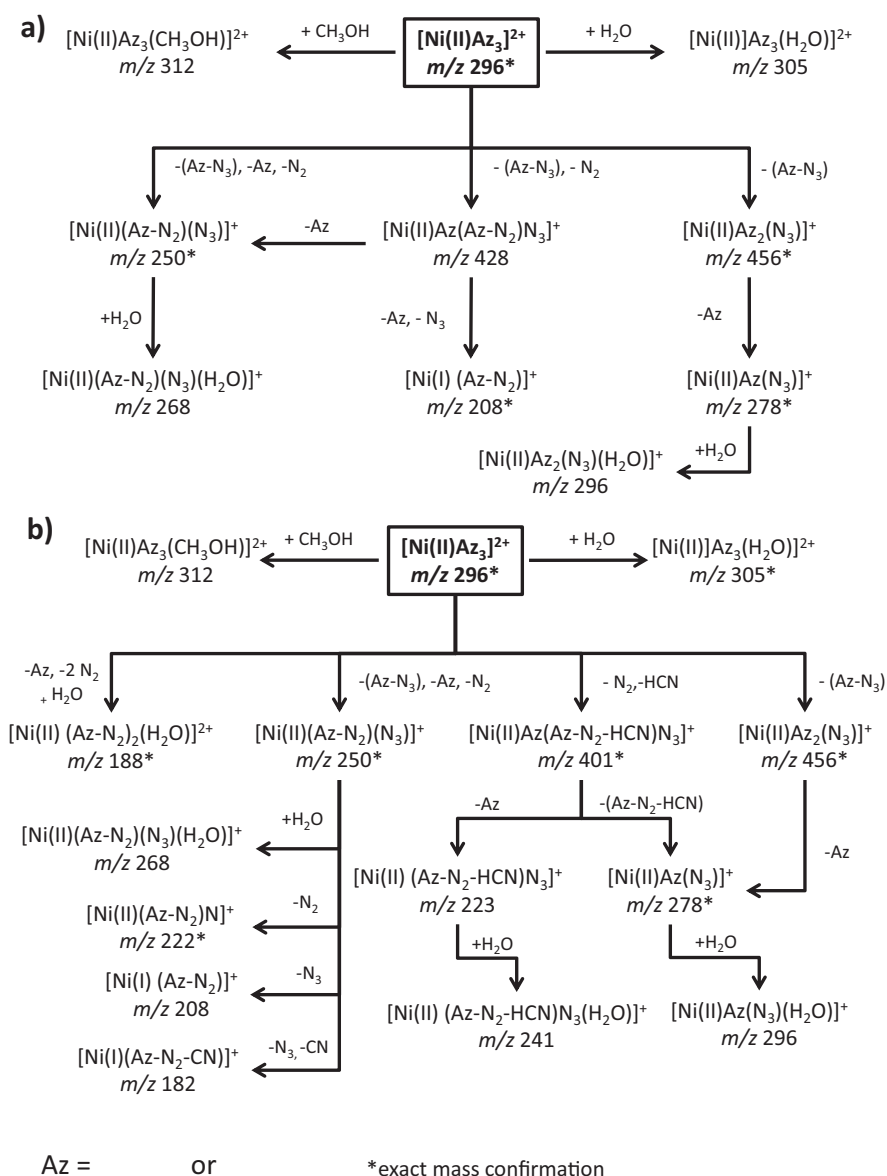
minima were found where one Az ligand also coordinates with both oxygen atoms of $-\text{NO}_2$ (**o.C**, **o.D**, **o.E**, and **o.G**), nickel having a square-planar coordination geometry with **o.C** being the most stable one. In this **o.C** conformation, all Az ligands are coordinated by the oxygen atoms of the $-\text{NO}_2$ groups in contrast with the lowest energy conformation **o.H** where two Az ligands are coordinated by the $-\text{N}_3$ group. The energy difference between both structures is 3.4 kJ mol^{−1}. The rather low energy difference between **o.C**, **o.D** and **o.H** structures (Fig. 3) may be indicative that they can co-exist in the gas-phase or even that an interconversion between them occurs after CID activation. The latter situation has been documented in the



Az =

*exact mass confirmation

Scheme 2. Proposed sequential fragmentation of the ion at m/z 296 for the *ortho*-nitrobenzyl azide.



Scheme 3. Proposed sequential fragmentation of the ion at m/z 296 for: (a) *meta*-nitrobenzyl azide and (b) *para*-nitrobenzyl azide.

literature for several transition metal complexes such as Cu(urea)⁺ [58], Ni(II)-ethylenediamine complexes [59], and peptides [60], just to name a few. The formation of the ion at m/z 179 by loss of one azide and two N₂ from ion at m/z 296 (Scheme 2) can be rationalized in terms of such an interconversion.

The *ortho*-nitrobenzyl azide molecule is also able to act as bidentate ligand, through their -NO₂ and -N₃ groups binding simultaneously, and this coordination mode was found in **o.A**, **o.B**, and **o.F** but they are higher in energy than the remaining conformations.

The same calculations were performed for the [Ni(II)Az₃]²⁺ ion containing *meta*-nitrobenzyl azide. The lowest energy conformer was **m.C** in which nickel is square-planar with four oxygen atoms in the coordination sphere; one *meta*-nitrobenzyl azide ligand coordinates by the two oxygen atoms of the -NO₂ group while the remaining ligands coordinate only by one oxygen. This structure is equivalent to **o.C** for the *ortho* ligand. In conformers **m.A** and **m.B** (Supplementary Information, Fig. S5), one *meta*-nitrobenzyl azide is bidentate, differing in the coordination mode of the other two ligands. Their energies are relatively high, especially when

compared with the *ortho*-analogues (**o.A** and **o.B**), indicating that the *meta*-position of the substituents might induce a higher strain on this coordination mode.

A very important conformer is **m.D**, which is related to **o.H** (and **o.G**). Contrary to what was found in the *ortho*-isomer, in **m.D** the Az ligand has no flexibility to allow the interaction of both dangling -NO₂ groups with the metal centre which remains free. This greatly increases its energy relative to **m.C** (104.2 kJ mol⁻¹). So, when comparing the *ortho*- and *meta*-isomers, it is clear that for *meta*-, coordination by the oxygen atoms of -NO₂ (one ligand using both atoms, the other two using only one) is preferred while for *ortho*-, although this coordination is possible (**o.C**), the preferred one involves one Az ligand coordinated by one -NO₂ group (using both oxygen atoms) and the other two coordinated by -N₃ (**o.H**). These differences should account for the different fragmentation patterns (see below).

For *para*-nitrobenzyl azide, bidentate coordination modes are not available due to the position of the substituents. Again, coordination by the -NO₂ of the three ligands appears to be the most favourable coordination mode (**p.B** conformer). This conformation

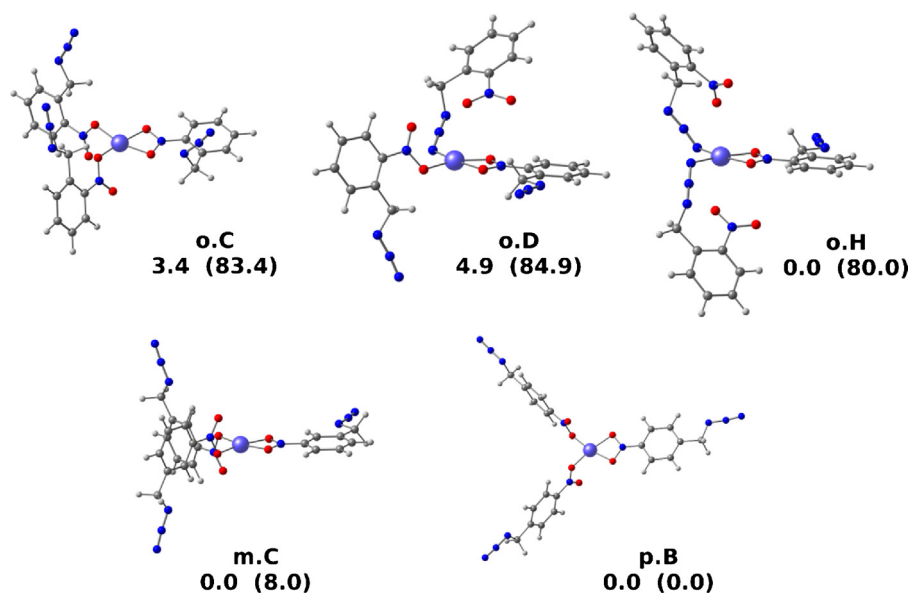


Fig. 3. Optimized lowest-energy conformations obtained for the $[\text{Ni}(\text{II})\text{Az}_3]^{2+}$ ion with Az = *ortho*-, *meta*-, *para*-nitrobenzyl azide. Energies (kJ mol^{-1}) relative to their respective isomer lowest energy conformation are given. In parenthesis the energies relative to the lowest-energy structure found in this study (p.B) are presented.

is the most stable one found in this study considering *ortho*-, *meta*-, and *para*-isomers in terms of absolute energies. Coordination through the N_γ of the $-\text{N}_3$ group results in a high energy structure, **p.A**, due to the incomplete coordination sphere of nickel (Supplementary Information, Fig. S6). As for *meta*-, it was not possible to obtain a structure equivalent to **o.H** in the *para*-isomer.

Although no definite answers arose from the calculations, some hints could be taken that could explain the different fragmentations observed for m/z 296 $[\text{Ni}(\text{II})\text{Az}_3]^{2+}$ with *ortho*-, *meta*-, and *para*-Az ligands. We have seen that several *ortho*-ligand complexes exist in the energy interval (0 – 31 kJ mol^{-1}) which could make difficult to undoubtedly assign a single structure for $[\text{Ni}(\text{II})\text{Az}_3]^{2+}$. In fact, the most stable conformer could be harder to fragment and the $[\text{Ni}(\text{II})\text{Az}_3]^{2+}$ ion could be a mixture of conformers. It is not hard to see that direct C– NO_2 bond cleavage, with loss of $\text{C}_6\text{H}_4\text{CH}_2\text{N}_3$, yielding the MS^2 product ion $[\text{Ni}(\text{II})\text{Az}_2(\text{NO}_2)]^{2+}$ observed at m/z 230 and confirmed by accurate mass measurements, is possible in conformers **o.B**, **o.C**, **o.D**, **o.E**, **o.F**, **o.G**, and **o.H** and therefore, it is not surprising that this loss is important for *ortho*- complexes. Moreover, the most striking difference between the *ortho*-isomer and the *meta*-/*para*- ones is the low-energy of conformer **o.H**, which has no equivalent in the *meta*- and *para*-Az ligands. Structurally this ion at m/z 230 must retain not only a coordinated $-\text{NO}_2$ group, but also, possibly, the nickel interaction with the other two “dangling” $-\text{NO}_2$ groups as in the most stable conformer **o.H**. This latter observation confirms the ability of electrospray ionization to transfer non-covalent interactions from solution to the gas-phase [54].

The loss of 92 Da yielding the ion at m/z 250 $[\text{Ni}(\text{II})(\text{Az}-\text{N}_2)\text{N}_3]^+$ in the *meta*-isomer is not as easily explained. This would require a C– N_3 bond cleavage, leaving the N_3 coordinated, plus the loss of one entire Az ligand and the loss of N_2 from the third Az. If one takes the **m.C** structure, it is possible to see that, both the loss of Az and N_2 are compatible. However, since Az is not coordinated by $-\text{N}_3$, C– N_3 bond cleavage, leaving the $\text{Ni}-\text{N}_3$ is not easily explained. One might postulate that after one Az ligand is lost, the completion of the coordination sphere is achieved by the rearrangement of the coordination of one Az ligand by both their $-\text{NO}_2$ and $-\text{N}_3$ groups. From this intermediate, it would be possible to cleave the C– N_3 bond forming the $[\text{Ni}(\text{II})(\text{Az}-\text{N}_2)\text{N}_3]^+$ ion. Another possibility is, as mentioned before, the participation of the higher energy structures which seem more favourable for this fragmentation. The same

could be also true for the *para*-isomer since in **p.B** the same coordination mode was found and should explain the similarities between *meta*- and *para*-behaviour while **o.H** is remarkably different.

As stated above, for $[\text{Ni}(\text{Az})_3]^{2+}$ complexes (high abundance ions) the coordination of the azide to the metal centre by the oxygen atoms of the NO_2 group and/or by the N_γ of the azido group leads to the energetically most favourable structures. On the other hand, for previously studied aliphatic azides [28,30] azidoacetone coordinates preferentially through the carbonyl and by the N_α of the azide group, giving rise to a stable five-membered structure [61]; 3-azidopropionitrile coordinates to the metal centre only through the nitrile group, which can be explained by the adequate symmetry of the CN antibonding orbitals to interact with the metal d orbitals, thus strengthening the metal–ligand bond [62]. Both aromatic azides and azidoacetone [30] tend to form chelates which stabilize the structure. This behaviour is favoured by the presence of groups with oxygen in both azides since Ni(II) has high affinity for oxygen ligands [63,64].

After analysing bifunctional aliphatic and aryl azides as ligands, it was not possible to establish a distinct trend in complexation sites. It is reasonable to assume that the participation of N_3 by N_α or N_γ in the complexation depends of the ligand's structure and, in this particular case, on the ring substituents. Furthermore, no evidence for the participation of the aromatic ring in the complexation was found.

4. Conclusions

This study aimed to make a contribution to the understanding of coordination in organoazidometal complexes, which have been investigated as intermediates in imidometal complex formation [21–26], as well as to distinguish the nitrobenzyl azides' isomers.

In this electrospray investigation of nitrobenzyl azides, singly and doubly charged complex ions, with different ligands and different stoichiometries, were detected. *Ortho*-nitrobenzyl and *para*-nitrobenzyl azides presented singly and doubly charged ions. Most of the singly charged ions in the *ortho*-isomer were due to the presence of Cl^-/Br^- as a ligand. Doubly charged ions were observed exclusively in *meta*-nitrobenzyl azide. The most

abundant complex ions had the general formula $[\text{Ni(II)Az}_3]^{2+}$ for *ortho*- and *para*-isomers and $[\text{Ni(II)Az}_3(\text{H}_2\text{O})]^{2+}$ for *meta*-isomer.

The different behaviour, of the three nitrobenzyl azides isomers' in the mass range m/z 296– m/z 312, detected in their mass spectra allows them to be distinguished. The MS^2 mass spectra of the ion at m/z 296, a common abundant ion, were investigated. This was useful to differentiate chiefly the *ortho*-isomer from the others. Due to the various coordination possibilities of these ligands, DFT calculations were performed which enabled the coordination mode to be clarified: for *ortho*-, a low-energy conformation was calculated which is not possible in the *meta*- and *para*-isomers: one Az ligand is coordinated by both oxygen atoms of the $-\text{NO}_2$ group while the remaining are coordinated by the $-\text{N}_3$, leaving two $-\text{NO}_2$ groups free to interact with the metal in the axial position. For *meta*- and *para*-, coordination by the oxygen atoms of the $-\text{NO}_2$ groups of the three ligands are more stable. These differences appear to be consistent with the fragmentation patterns observed experimentally.

Considering the loss of N_2 in *ortho*-isomer, leading to m/z 179, and coordination by N_3 in the *meta*- and *para*-isomers leading to the formation of m/z 456, 428, 401, 250, under collision-induced dissociation conditions, either a conversion to a more energetic structure or a co-existence of structures must occur.

As a general trend, for the three isomers, the $-\text{NO}_2$ group is always coordinated to the nickel by two oxygen atoms in the most stable conformations. On the other hand, the azido group coordinates, when involved in the coordination, to the metal through the terminal nitrogen (N_γ) not through the alkylated one (N_α). In addition, the chelation effect detected for azidoacetone [32] was not observed in the most stable conformations for nitrobenzylazides. Moreover, unlike for 3-azidopropionitrile and azidoacetone [30], for the three nitrobenzyl azide isomers no evidence was found for C–C bond activation and metal insertion.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ijms.2013.05.012>.

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