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Protonated *N*-Alkyl-2-nitroanilines Undergo Intramolecular Oxidation of the Alkyl Chain upon Collisional Activation

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Abstract

The collisional activation of protonated *N*-propyl-2-nitroaniline obtained by electrospray ionization shows two major competitive dissociation pathways: the elimination of the elements of propionic acid, $[M + H - C_3H_6O_2]^+$ to give an m/z 107 ion, and of the elements of ethanol, $[M + H - C_2H_6O]^+$ to give an m/z 135 ion. The mechanistic study reported here addresses these unusual fragmentations to reveal that both occur via a common intermediate formed by the transfer of an oxygen atom from the nitro group to the first carbon atom of the propyl group, allowing elimination of propionic acid and (H_2O + ethene), respectively. The corresponding loss of CH_4O does not occur when the propyl group is replaced by an ethyl group, but elimination of the elements of propanol does occur when propyl is replaced by a butyl group. Further, the product ions of m/z 107 and 135 are also formed when the propyl chain is replaced with a hexyl group.

Keywords

collisional activation; intramolecular oxidation; oxygen atom rearrangement; nitro group; protonated *N*-alkyl-2-nitroaniline; density functional theory; mass spectrometry

1. Introduction

Intramolecular oxygen transfer from a nitro group to other parts of the molecule leading to redox reactions mediated by transition metal ions are known to occur in both solution [1,2] and the gas phase [3]. These oxygen transfers from a nitro group are important in synthetic organic chemistry [4] and in biological transformations [5]. Turecek and coworkers used tandem mass spectrometry in combination with density functional theory to study an

oxygen-transfer, gas-phase reaction giving the elimination of H_2CO_3 from an ionized copper complex of nitro tyrosine [3]. The electron-ionization (EI) induced oxygen transfer from a nitro group leading to intramolecular oxidation of sulfur, alkyl or alkenyl groups in aromatic nitro compounds is well established [6,7]. The intramolecular oxidation involves either the transfer of oxygen atoms from the nitro group to the heteroatom or side chain [6] within the radical cation or the abstraction of hydrogen atoms from the side chain to the nitro group. The process leads to the elimination of small molecules via a process termed an ortho effect [7]. Such rearrangements are not common for protonated molecules (closed-shell ions) generated by electrospray ionization (ESI) and activated in low-energy collisions, probably owing to the absence of a radical site. Nevertheless, we previously found an example of intramolecular oxidation of a sulfur atom by an adjoining nitro group for the ESI-protonated 2-nitrophenylphenylsulfide, and we characterized the chemical reactions by experiment supported by theoretical calculations [8].

Others showed that the EI-generated radical cation of *N*-ethyl-2-nitroaniline eliminates a molecule of acetic acid [9, 10], and, to a small extent, a molecule likely to be acetaldehyde. In an analogous manner, the molecular radical cations of propyl and butyl amines fragment via eliminations of propionic acid and butyric acid, respectively. The mechanism suggested for these gas-phase eliminations of the alkyl group attached to the nitrogen as a carboxylic acid, involves the oxidation of the alkyl group by the ortho nitro group. Do these intramolecular oxidation reactions of nitro group, observed for open-shell ions, occur as analogous reactions in closed-shell, $[\text{M} + \text{H}]^+$ ions generated by ESI? The answer is important because ESI mass spectrometry has now become the method of choice for the analysis of most organic compounds and pharmaceuticals.

We report here an experimental and theoretical investigation of the collision-activated dissociations of the ESI-generated $[\text{M} + \text{H}]^+$ ions of *N*-ethyl-2-nitroaniline (**1**), *N*-propyl-2-nitroaniline (**2**), *N*-butyl-2-nitroaniline (**3**), *N*-hexyl-2-nitroaniline (**4**), and *N*-butyl-4-chloro-2-nitroaniline (**5**). The goal is to understand the possibility of intramolecular oxygen transfer reactions by nitro groups, leading to eliminations of alkanic acids. We augmented the experimental observations by carrying out density function theory (DFT) calculations to explore the mechanism of oxygen transfer.

We are pleased to dedicate this article to the late Nico M.M. Nibbering, a close friend and colleague whose enthusiastic commitment to ion chemistry continues to be inspirational. The dedication of this paper is indeed appropriate because his first published work focused on the role of the nitro group in the McLafferty rearrangement of the nitropropane radical cation [11], a study that was always a source of pride to him. This work shows another

property of the nitro group in gas-phase ion chemistry, and we are certain that the unusual rearrangement via intramolecular redox chemistry would interest him.

2. Materials and methods

2.1 Synthesis

Compounds **1-4** were prepared by treating a solution of 1-fluoro-2-nitrobenzene (1.0 g) in 10 mL 1,4-dioxane with excess (3 mL) of the appropriate alkyl amine at room temperature, analogous to the synthesis of *N*-(2-nitrophenyl)benzylamine [12]. Compound **5** was synthesized by refluxing 2,4-dichloronitrobenzene (1.0 g) with butyl amine (3 mL) in 1,4-dioxane. The reactions were completed in 2 h, and the mixture was diluted with 50 mL water and extracted with dichloromethane (2×50 mL). Dichloromethane was removed by distillation at reduced pressure, and the products were purified by column chromatography on silica gel using hexane and chloroform (9:1) as eluent. The structures were confirmed by their NMR and accurate mass ESI mass spectra.

2.2 Mass spectrometry

ESI mass spectra of the compounds were obtained by direct infusion (5 μ L/min) using a dilute solution of the amines in a 1:1 mixture of acetonitrile/water. The low mass resolving-power MS and CAD (MS/MS) experiments using helium as collision gas were performed with a Thermo LCQ Deca Ion-Trap (San Jose, CA) mass spectrometer operated in the positive-ion mode. Dry nitrogen gas at 90 $^{\circ}$ C was used for desolvation. High mass resolving-power CAD (collision gas – helium) experiments were performed with a Thermo LTQ-Orbitrap mass spectrometer operated in the positive-ion mode (resolving power for product ions was 30,000 for MS/MS). The collision energy was adjusted to keep the abundances of the precursor ion and the most abundant product ion to be similar.

2.3 Theoretical calculations

Theoretical calculations were performed on compound **2** to characterize the potential-energy surface (PES) associated with its fragmentation. Conformer spaces for putative precursors and products were explored by Monte-Carlo/MMFF molecular mechanics/dynamics methods. From these results, structures of precursors, intermediates, and scans for associated transition states were explored by using the PM3 semi-empirical [13, 14] algorithm (Spartan for Linux: Wavefunction, Inc.), and if necessary, scans were also performed by DFT: B3LYP/6–31G(d,p). The minima and transition states so obtained were geometrically optimized by DFT (Density Functional Theory, part of Gaussian 03/09 suites [15, 16] (Gaussian Inc., Wallingford, CT) to level B3LYP/6–31G(d,p) and confirmed by vibrational frequency analysis (geometries in Supplementary Data – Table S2). Connections of transition states to minima projections along normal-reaction coordinates, and path calculations were examined by inspection, as necessary. Discovered also by path calculations were ion-dipole complexes. Single-point energies were calculated at B3LYP/6–311++G(3df,2p)//B3LYP/6–31G(d,p) level and scaled thermal-energy corrections for standard conditions were applied [17]. DFT was selected for high-level calculations because it required less computational overhead than *ab initio* methods and performed adequately [18]. All calculated enthalpies were determined as relative to an initial form of protonated

compound **2**, **M0**, and expressed in kJ/mol (reported in Table 2 and Supplementary Data - Table S1).

3. Results and Discussion

3.1 Mass spectrometry

ESI of *N*-ethyl-2-nitroaniline (**1**) showed that the $[M + H]^+$ ion of m/z 167, upon collisional activation dissociated to yield product ions of m/z 107 and less abundant ions of m/z 149 by eliminating species of 60 ($C_2H_4O_2$) and 18 u (H_2O), respectively (Fig. 1). We assigned the elemental compositions of the $[M + H]^+$ and its fragment ions, by repeating the experiments on an instrument capable of high mass resolving power and accurate mass measurement (Table 1) to confirm that the unexpected fragment ion of m/z 107 is formed by the elimination of $C_2H_4O_2$, probably a molecule of acetic acid (Scheme 1). In addition, the elemental composition of the fragment ion of m/z 149 confirms the elimination of H_2O from the protonated molecule. The elimination of acetic acid, suggests that the nitro group, upon protonation, can oxidize the ethyl group attached to the amino group in a process similar to the fragmentation of the same compound upon EI [10].

To understand further the oxidation of the *N*-alkyl group, we obtained the ESI mass spectrum of *N*-propyl-2-nitroaniline (**2**), a molecule having a longer alkyl chain by a methylene unit. The CAD mass spectrum of the $[M + H]^+$ shows reactions to give major fragment ions of m/z 135 and 107 by eliminations of 46 u and 74 u, respectively (Fig. 1b). The elemental compositions confirm that these fragment ions are formed by the eliminations of C_2H_6O and $C_3H_6O_2$, the elements of ethanol and propanoic acid, respectively, Table 1, Scheme 2. Hence the rearrangement that occurs for protonated *N*-propyl-2-nitroaniline causes the oxidation of both first and second carbon atoms of the alkyl chain.

To understand the oxidation process, we examined the ESI mass spectra of compounds **3** and **4** containing, respectively, a butyl and a hexyl group attached to the nitrogen atom. The $[M + H]^+$ ion of **3**, *N*-butyl-2-nitroaniline, dissociates by the competitive eliminations of the elements of butanoic acid and propanol, whereas the $[M + H]^+$ ion of **4** (*N*-hexyl-2-nitroaniline) eliminates the elements of hexanoic acid and pentanol. Upon collisional activation, the $[M + H]^+$ ions of compounds **3** and **4** dissociate via eliminations of carboxylic acids containing the same number of carbons as the alkyl chain and alcohols containing one carbon less than the full alkyl chain (Fig. 2), indicating that the oxygen transfers can occur to either the first or second carbon of the alkyl chain. Moreover, the $[M + H]^+$ ion of *N*-butyl-4-chloro-2-nitroaniline (**5**) dissociates via eliminations of the elements of butanoic acid and propanol (Fig. 2b), analogous to the fragmentations of protonated **3**. The measured accurate masses give elemental compositions of the protonated molecules and the fragment ions that are consistent with these processes (Table 1).

3.2 DFT calculations

We submitted the smallest compound that shows both alkanolic acid and alcohol eliminations (i.e., *N*-propyl-2-nitroaniline) to DFT calculations to probe the mechanisms of the dissociation. Calculations show both the NH nitrogen and the oxygen of the NO_2 group are

protonation sites for *N*-propyl-2-nitroaniline (Scheme 3, Table 2). The O-protonated species **M1** has four potential conformations, one unstable and another metastable. In the lower energy conformation, the alkyl group and the free O-atom of the NO₂ group are too remote for any interaction, but in the higher energy rotational isomer, the O-atom is close to an H-atom of the first CH₂ group of the propyl group (the optimized structure and relative energies of the N-protonated and the three O-protonated structures of the [M + H]⁺ ion are in Table 2 and Scheme 3).

The O-protonated species **M2** is the entry point for the internal oxygen transfer and fragmentation processes. The shift of a proton from **M0** to **M2** requires 146 kJ/mol via TS(0–2) and 135 kJ/mol through **M1s** and **M1**, but obtaining **M2** from **M1** via TS(1–2) requires only 29 kJ/mol. The former large differences are consistent with the large difference in the proton affinity of nitrobenzene vs that of aniline, whereas the latter suggest restricted rotation likely due to some double-bond character between the N of protonated NO₂ and the aromatic ring. The energy required for the first step of the transfer/fragmentation channel via TS(2–3) requires 132 kJ/mol. Thus, nearly all these N and O protonated species would be available to an activated species undergoing transfer of the OH group (Scheme 4).

We propose that, consistent with theory, the first step in the oxygen transfer and fragmentation involves the unprotonated oxygen atom of nitro group of the O-protonated species **M2** abstracting a hydride ion from the first CH₂ group of the alkyl group. The resulting species, **M3**, further rearranges by the migration of a hydroxyl anion from the N to the CH, to form intermediate **M4** and accomplish the transfer of an oxygen from the nitro group to the first carbon of the alkyl group, Scheme 4. A suprafacial 1,5 H-shift followed by a 1,6 H-shift transforms the intermediate **M4** to **M6**. The competitive eliminations of the elements of propanoic acid and propanol occur from **M6**.

The transfer of an H-atom from carbon-3 of the propanoyl group (originally the propyl group) to the OH group transforms **M6** into an ion-dipole complex (**IDC1**) of the product ion **M7** and the neutral molecule H₂O. An intramolecular nucleophilic displacement of an ethylene molecule by the NH₂ group within intermediate **M7**, after the elimination of H₂O, generates another ion-dipole complex, **IDC2**, consisting of neutral ethylene and **M8**, which is the product ion of *m/z* 135 after elimination of ethylene. As evidence for the sequential loss of water and ethylene, note that the transition barrier between **M6** and **M7** is substantial, but that between **M7** and **M8** is very small, and the energetics trajectory is downward to lower enthalpies (Fig. 3). In addition, as seen in Fig. 1b, the product-ion spectrum of the [M + H]⁺ of **2**, there is a low abundance ion at *m/z* 163 formed by water loss as expected for the energetics of the trajectory. Additional evidence is the product-ion spectrum of [M + H]⁺ of **1** (Fig. 1a) that shows facile losses of water and acetic acid but no loss of methanol or its equivalence; that loss would require the elimination of the methylene (carbene), a high-energy product.

The combined elimination of H₂O and C₂H₄ is formally equivalent to the elimination of ethanol, but the proposed mechanism shows that the elimination of the elements of alcohol is possible only if the alkyl chain has a minimum of three carbon atoms. Thus, this proposed mechanism explains the absence of methanol elimination in the CAD mass spectrum the [M

+ H]⁺ ion of *N*-ethyl-2-nitroaniline (**1**). In a competing process, the transfer of a hydroxyl group from the NH₂-OH group to the carbonyl group leads to the elimination of propanoic acid to yield an ion of *m/z* 107 with a proposed structure of **M9**. Note that for this product ion, the original nitro group is completely reduced to an amine.

A potential energy diagram of the various intermediates and transition states described in Scheme 4 are depicted in Fig. 3 and the relative enthalpies are given in Table 2. The major transition states for both routes from **M6** occur at **M6** and are similar in barrier enthalpy, consistent with the comparably abundant product ions found in the CAD spectrum of **2**.

4. Conclusion

The [M + H]⁺ ions of the *N*-alkyl-2-nitroanilines undergo unusual oxidation reactions of the alkyl side chains as seen in the CAD (MS/MS) spectrum and confirmed by DFT calculations. Specifically, a shift of the proton of the activated species to the nitro group leads to the intramolecular oxidation of *N*-alkyl chain with concomitant reduction of the nitro group and elimination of an alkanic acid with the same number of carbon atoms as in the alkyl chain. Furthermore, when the alkyl chain contains more than two carbon atoms (compounds **2** to **5**), the protonated molecule undergoes competitive eliminations of the elements of an alcohol with one carbon less than the alkyl group. DFT calculations reveal that the elimination is likely a sequential loss of H₂O and a 1-alkene rather than an alcohol. An interesting question is whether these protonated species in solution can be induced to undergo similar oxidations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Kovalevsky AY, King G, Bagley KA, and Coppens P, Chem. Eur. J 2005, 11, 7254–7264. Photoinduced Oxygen Transfer and Double-Linkage Isomerism in a cis-(NO)(NO₂) Transition-Metal Complex by Photocrystallography, FT-IR Spectroscopy and DFT Calculations. 10.1002/chem.200500653 [PubMed: 16187381]
2. Li X, Incarvito CD, Vogel T, and Crabtree RH, Organometallics 2005, 24, 3066–3073. Intramolecular Oxygen Transfer from Nitro Groups to Carbon Carbon triple Bonds Mediated by Iridium Hydrides. DOI: 10.1021/om050116+
3. vaisar T, Heinecke JW, Seymour JL, Turecek F, J. Mass Spectrom, 2005, 40, 608–614. Copper-mediated intra-ligand oxygen transfer in gas-phase complexes with 3-nitrotyrosine. 10.1002/jms.829 [PubMed: 15724273]
4. Baricelli PJ, Castillo A, Longo C, Pardey AJ, React. Kinet. Catal. Lett 2000, 70(1), 133–38. Homogeneous catalytic oxidation of cyclohexene by nitro complexes of copper (II). 10.1023/A:1010327119019

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5. Korvekandi H, Mather P, Gardiner J, Stephens G, Enzyme and Microbial Technology, 2008, 42, 308–14. Reduction of aliphatic nitro groups using an obligately anaerobic whole cell biocatalyst. 10.1016/j.enzmictec.2007.10.009
 6. Ramana DV, Sundaram N, George M, Org. Mass Spectrom 25 (3) (1990) 161–164. Ortho effects in organic molecules on electron impact. Part 22. Competing oxygen transfers from the nitro group to sulfur and the olefinic double bond in 2-nitrophenyl styryl sulfides. 10.1002/oms.1210250308
 7. Lambert P-H, Bertin S, Lacoste J-M, Volland J-P, Krick A, Furet E, Botrel A, Guenot P, J. Mass Spectrom. 1998 33(3), 242–249. Electron ionization-induced loss of SO₂ from 2-nitrodiaryl sulfides. 10.1002/(SICI)1096-9888(199803)33:3<242::AID-JMS627>3.0.CO;2-G
 8. Moolayil JT, George M, Giblin D, Gross ML, 2009 Inter. J. Mass Spectrom, 283(1–3), 222–228. 2-Nitrophenyl aryl sulfides undergo both intramolecular and electrospray-induced intermolecular oxidation of sulfur: An experimental and theoretical case study. 10.1016/j.ijms.2009.04.003
 9. Danikiewicz W, Rapid Commun. Mass Spectrom, 1998 12(11), 689–694. Formation of benzimidazole derivatives during electron ionization induced fragmentation and pyrolysis of N-benzyl-o-nitroaniline. 10.1002/(SICI)1097-0231(19980615)12:11<689::AID-RCM219>3.0.CO;2-2
 10. Danikiewicz W, Mass Spectrom J, 1998 33(11), 1063–1070. tert-Amino effect following electron ionization of N,N-dialkyl-o-nitroanilines. 10.1002/(SICI)1096-9888(1998110)33:11<1063::AID-JMS708>3.0.CO;2-A
 11. Nibbering NMM, De Boer TJ, Hofman HJ, Rec. Trav. Chim. Pays-Bas, 1965, 84(4), 481–487. Mass Spectrometry of Nitro Compounds. Part I. Mass spectra of α -, β -, and γ -Deuterated 1-Nitropropane. 10.1002/recl.19650840412
 12. Gardiner JM, Goss AD, Majid T, Morley AD, Pritchard RG and Warrena JE, Tetrahedron Lett. 2002, 43(43), 7707–7710. Synthesis of N-alkoxybenzimidazoles and N-alkoxyimidazoles. 10.1016/S0040-4039(02)01841-5
 13. Stewart JJP, J. Comp. Chem 1989, 10(2), 209–220. Optimization of parameters for semiempirical methods I. Method. 10(2), 209–220. 10.1002/jcc.540100208
 14. Stewart JJP, J. Comp. Chem 1989, 10(2), 221–264. Optimization of parameters for semiempirical methods II. Applications. 10.1002/jcc.540100209
 15. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Montgomery JA Jr., Vreven T, Kudin KN, Burant JC, Millam JM, Iyengar SS, Tomasi J, Barone V, Mennucci B, Cossi M, Scalmani G, Rega N, Petersson GA, Nakatsuji H, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Klene M, Li X, Knox JE, Hratchian HP, Cross JB, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Ayala PY, Morokuma K, Voth GA, Salvador P, Dannenberg JJ, Zakrzewski VG, Dapprich S, Daniels AD, Strain MC, Farkas O, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Ortiz JV, Cui Q, Baboul AG, Clifford S, Cioslowski J, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Gonzalez C, J. A. Pople, Gaussian 03, Revision C.02, Gaussian, Inc, Wallingford CT, 2004.
 16. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JA Jr., Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam JM, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas O, Foresman JB, Ortiz JV, Cioslowski J, and Fox DJ, Gaussian 09, Revision A.02, Gaussian, Inc., Wallingford CT, 2009.
 17. Scott, Radom L, J. Phys. Chem, 1996, 100, 16502–13. Harmonic Vibrational Frequencies: An Evaluation of Hartree-Fock, Møller-Plesset, Quadratic Configuration Interaction, Density Functional Theory, and Semiempirical Scale Factors. <http://pubs.acs.org/doi/abs/10.1021/jp960976r>

18. Shephard MJ, Paddon-Row MN, J. Phys. Chem 1995 99(10), 3101–3108. Gas Phase Structure of the Bicyclo[2.2.1]heptane (Norbornane) Cation Radical: A Combined ab Initio MO and Density Functional Study. 10.1021/j100010a020

Fig.1.
CAD mass spectra (by MS/MS) of the ESI produced $[M + H]^+$ ion of (a) compound **1** and (b) compound **2**.

Fig. 2.
CAD mass spectra of ESI-produced $[M + H]^+$ ion of (a) compound **3** and (b) compound **5**.

Fig. 3:
Comparative enthalpies of formation along the reaction trajectories for compound 2
(Scheme 3 & 4) in kJ/mol.

Scheme 1. Significant fragmentations of the $[M+H]^+$ ion of compound **1**.

Scheme 2.

Significant fragmentations of the [M+H]⁺ ion of compound 2.

Scheme 3:

Mechanism for fragmentation of protonated compound 2.

Scheme 4:

Proposed mechanism of fragmentation by competitive losses of propionic acid and ethanol via equivalent consecutive losses of H₂O and ethylene from compound **2**.

Table 1.

Elemental compositions of the $[M + H]^+$ and CAD fragment ions of compounds **1-5**. The figures in parentheses are calculated masses and % relative abundances.

Compound	$[M + H]^+$	$[M + H - H_2O]$	$[M + H - ROH]^+$	$[M + H - RCOOH]^+$
<i>N</i> -ethyl-2-nitroaniline (1)	C ₈ H ₁₁ N ₂ O ₂ 167.0810 (167.0815)	C ₈ H ₉ N ₂ O 149.0705 (149.0709)(20)	not detected	C ₆ H ₇ N ₂ 107.0599 (107.0604) (100)
<i>N</i> -propyl-2-nitroaniline (2)	C ₉ H ₁₃ N ₂ O ₂ 181.0970 (181.0972)		C ₇ H ₇ N ₂ O 135.0550 (135.0553)(92)	C ₆ H ₇ N ₂ 107.0603 (107.0604) (100)
<i>N</i> -butyl-2-nitroaniline (3)	C ₁₀ H ₁₅ N ₂ O ₂ 195.1127 (195.1128)		C ₇ H ₇ N ₂ O 135.0552 (135.0553) (100)	C ₆ H ₇ N ₂ 107.0603 (107.0604)(93)
<i>N</i> -hexyl-2-nitroaniline (4)	C ₁₂ H ₁₉ N ₂ O ₂ 223.1442 (223.1441)		C ₇ H ₇ N ₂ O 135.0552 (135.0553)(100)	C ₆ H ₇ N ₂ 107.0604 (107.0604)(68)
<i>N</i> -butyl-4-chloro-2-nitroaniline (5)	C ₁₀ H ₁₄ N ₂ O ₂ Cl 229.0741 (229.0738)		C ₇ H ₆ N ₂ OCl 169.0167 (169.0163)(60)	C ₆ H ₆ N ₂ Cl 141.0213 (141.0214)(100)

Table 2:Calculated relative enthalpies of formation/reaction for compound **2** (Schemes 3 and 4, in kJ/mol).

	Corr. H	H_f	H_{rxn}	H_{rxn2}
Label	(hartree)	(kJ/mol)	(kJ/mol)	(kJ/mol)
M0	-610.382760	0		
M1s	-610.375875	18		
M1	-610.383302	-1		
M2	-610.370865	31		
M3	-610.382039	2		
M4	-610.410025	-72		
M5	-610.439564	-149		
M5r	-610.434429	-136		
M6	-610.456360	-193		
M7	-533.987985		-114	
M8	-455.454072			-198
M9	-342.063228		-211	
IDC1	-610.436257	-140		
IDC2	-534.027817		-218	
IDC3	-610.488304	-277		
TS(0-0)	-610.367578	40		
TS(0-2)	-610.326681	147		
TS(0-1s)	-610.357117	67		
TS(1s-1)	-610.330946	136		
TS(1-2)	-610.371452	30		
TS(2-3)	-610.332182	133		
TS(3-4)	-610.341208	109		
TS(4-5)	-610.359414	61		
TS(5-5r)	-610.424899	-111		
TS(5r-6)	-610.409660	-71		
TS(6-IDC1)	-610.385794	-8		
TS(6-IDC3)	-610.381658	3		
TS(7-IDC2)	-533.986778		-111	
Ethanol	-155.019481			
Ethylene	-78.566024			
H2O	-76.438149			
Propionic Acid	-268.399900			