

Unusual nucleophilic versus electrophilic aromatic substitution on nitroanilines

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Abstract

The reaction of the regioisomeric nitroanilines with KI and HNO₃/bentonite system using microwave energy in solvent-free conditions is reported. In accordance with the obtained results, an unusual competence between nucleophilic aromatic substitution versus electrophilic aromatic substitution was detected. With the *para* isomer two products were obtained, one for each reaction type; however, with the *meta*-nitroaniline, only the nucleophilic substitution product was detected, and finally with the *ortho* isomer in addition to the nucleophilic and electrophilic substitution products, we detected the formation of 2,4-diiodonitrobenzene. In order to explain the achieved products, we propose that the last product is formed in two steps: firstly by a nucleophilic aromatic substitution, and secondly by an electrophilic aromatic substitution. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

Aromatic iodides have long been employed as intermediates in organic synthesis, thus several studies have been performed in order to obtain them [1–5]. However, the moderated reactivity of iodine with aromatic substrates requires the presence of an oxidizing

agent, a base, an activating medium or an iodonium donating reagent [6].

In addition, one of the most known methods to achieve this class of compounds is the Tronov–Novikov reaction [7], which consist of a mixture of nitric, sulfuric and acetic acid in the presence of iodine; the resulting sulfonitric mixture provides NO₂⁺, an oxidizing agent, which in turn promotes the formation of I⁺.

Related with our research program, we have been interested in the development of new organic synthetic

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strategies with the use of a bentonitic earth (TAFF)², as catalyst and/or medium of reaction in solvent-free systems, using microwave or infrared irradiations as energy sources [8–10]. Thus using the clay, in this paper, we discuss the obtained results for a set of reactions with KI in the presence of HNO₃/bentonite, with the three regioisomeric nitroanilines in absence of solvent under the employment of microwave energy. It is worth mentioning that the simplicity of the experimental conditions, the ease of workup to isolate the final products and the availability of the clay, makes this method feasible and advantageous to introduce a iodine atom in an aromatic ring.

2. Experimental

2.1. Materials and apparatus

Regioisomeric nitroanilines (Aldrich) were crystallized prior to use. The natural clay was obtained from Tonsil Mexicana and analyzed prior to use (see footnote 2). Purified products were characterized by spectroscopic means: ¹H NMR spectra were recorded in a Varian Gemini-300 spectrometer using CDCl₃ as solvent and TMS as internal reference; EI-MS (70 eV) spectra were obtained using JEOL MS AX 505 HA and MS-SM 102 mass spectrometers. The microwave irradiations were realized in a Kenmore 569978018 oven at 2459 MHz. Thin layer chromatographic analyses were realized using Merck precoated plates (silica gel 60 F₂₅₄, 0.25 mm) and for column chromatographies (flash) silica gel Merck 230–400 mesh was employed.

²Clay used is Tonsil Actisil FF (commercial name from Tosil Mexicana, S.A. de C.V.). On examination by X-ray fluorescence, the clay was found to have the following composition (in %): SiO₂, 63.5; Al₂O₃, 12.7; MgO, 3.1; Fe₂O₃, 4.9; CaO, 1.5; K₂O, 3.1; TiO₂, 0.6; MnO, 0.03; Na₂O, 0.8; P₂O₅, 0.1; H₂O (110°) 9.5. The material was analyzed with a Phillips spectrometer using Cr primary radiation. Quartz and cristobalite are also important components in the clay composition. The measured specific surface area was 161.074 m²/g (BET. N₂), and the pore volume was 0.3235 cm³/g. The acidity by NH₃ thermodesorption was 12.107 mmol/mg. The particle size was 325 mesh. Commercial price to date: US\$ 0.35/kg.

2.2. Experimental procedure for the preparation of HNO₃/bentonite system

Concentrated HNO₃ (60 ml) and bentonitic clay (50 g) were mixed and magnetically stirred over the night at room temperature. Then, the solid was filtered and dried in vacuo until a dust was obtained³.

2.3. Typical experiment

Equimolar amounts (10 mmol) of KI and nitroaniline with the HNO₃/bentonite system (1:10 ratio) were perfectly mixed in solvent-free conditions. Then, the resulting mixture was irradiated in a microwave domestic oven for 10 min. After this time, there were no remarkable worth-noting changes in all reactions. Then, the reaction mixture was extracted in Soxhlet apparatus for 2 h using ethyl acetate as solvent. The obtained extract was purified by chromatography.

2.4. Spectroscopic data

2.4.1. Compound 1: *p*-iodonitrobenzene

Pale yellow solid; mp 173°C; IR ν cm⁻¹: 3094.6 (C–H, Ar), 1597.9 and 1573.7 (C=C, Ar), 1518.9 and 1343.1 (–NO₂), 852.5 and 741.2 (*p*-substituted phenyl); EI-MS 70 eV m/z (% ra): 249 (100) M⁺, 219 (26) [M–30]⁺, 203 (35) [M–46]⁺, 191 (14) [M–58]⁺, 76 (60) [M–173]⁺, 50 (40) [M–199]⁺; ¹H NMR (CDCl₃) δ (ppm): 8.01 and 8.09 (4H, AA'BB', $J=9.36$ Hz).

2.4.2. Compound 2: 2-iodo-4-nitroaniline

Red solid; mp 173°C; IR ν cm⁻¹: 3471.3, 3372.3, (NH₂), 1622.5 (C=C, Ar), 1483.4 and 1307.8 (NO₂); EI-MS 70 eV m/z (% ra): 264 (100) M⁺; 248 (4) [M–16]⁺; 234 (41) [M–30]⁺; 218 (15) [M–46]⁺; 206 (4) [M–58]⁺; 137 (1) [M–127]⁺, 107 (8) [M–157]⁺; 91 (61) [M–173]⁺; ¹H NMR (CDCl₃) δ (ppm): 4.82 (2H, NH₂), 6.69 (d, 1H, Ar, $J=9.00$ Hz), 8.04 (dd, 1H, Ar, $J_1=2.49$ Hz, $J_2=9.00$ Hz), 8.56 (d, 1H, Ar, $J=2.49$ Hz).

³The measured acidity by NH₃ thermodesorption was 202 mmol/mg.

2.4.3. Compound 3: *m*-iodonitrobenzene

Pale brown solid; mp 31–33°C. IR ν cm^{-1} : 3096.1 (C–H, Ar), 1455.8, (C=C, Ar), 1534.1 and 1347.8 (NO_2), 864.8, 808.3, 772.5, 728.7; EI-MS 70 eV m/z (% ra): 249 (100) M^+ ; 219 (5) $[\text{M}-30]^+$; 203 (43) $[\text{M}-46]^+$; 191 (4) $[\text{M}-58]^+$; 76 (46) $[\text{M}-173]^+$; ^1H NMR (CDCl_3) δ (ppm): 7.35 (dd, 1H, $J_1=8.26$ Hz, $J_2=7.98$ Hz), 8.09 (m, 1H, $J_1=7.98$ Hz, $J_2=1.65$ Hz, $J_3=1.10$ Hz), 8.18 (m, 1H, $J_1=8.26$ Hz, $J_2=2.20$ Hz, $J_3=1.10$ Hz), 8.51 (t, 1H, $J_1=1.93$ Hz, $J_2=1.93$ Hz).

2.4.4. Compound 4: 2,4-diiodonitrobenzene

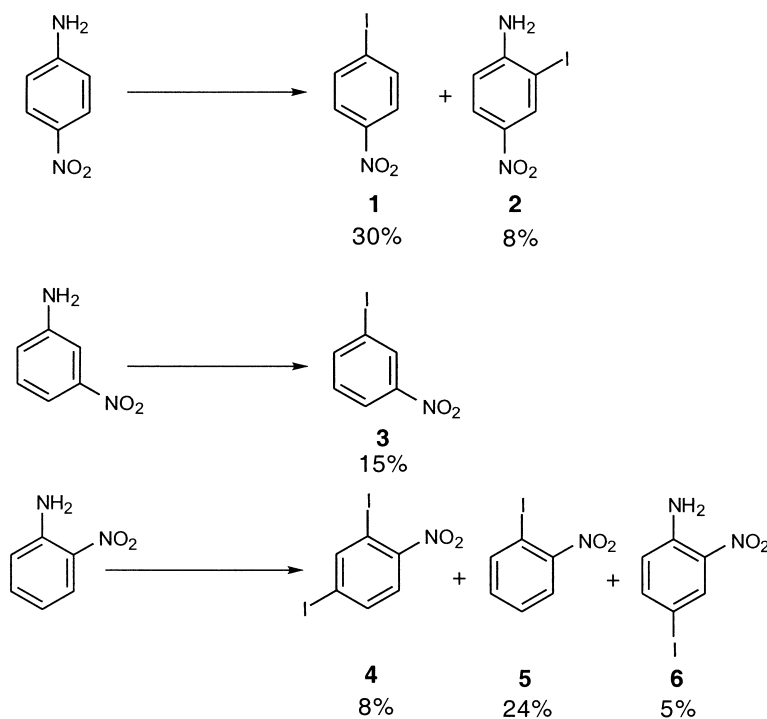
Pale yellow solid; mp 93–95°C. IR ν cm^{-1} : 3076 (C–H, Ar), 1565.6. (C=C, Ar), 1524.7 and 1348.4 ($-\text{NO}_2$), 865.6, 817.3. EI-MS 70 eV m/z (% ra): 375 (100) M^+ ; 329 (42) $[\text{M}-46]^+$; 218 (11) $[\text{M}-157]^+$; 202 (24) $[\text{M}-173]^+$; 75 (49) $[\text{M}-300]^+$; ^1H NMR (CDCl_3) δ (ppm): 7.56 (dd, 1H, $J_1=1.93$ Hz, $J_2=8.26$ Hz), 7.73 (d, 1H, $J=8.26$ Hz), 8.14 (d, 1H, $J=1.93$ Hz).

2.4.5. Compound 5: *o*-iodonitrobenzene

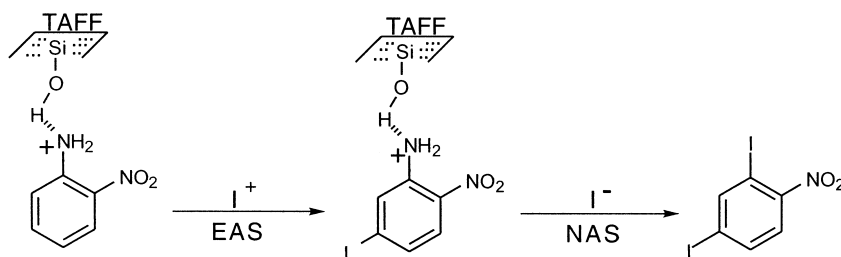
Yellow solid; mp 46–48°C. IR ν cm^{-1} : 1582.9 (C=C, Ar), 1521.8 and 1333.7 ($-\text{NO}_2$); EI-MS 70 eV m/z (% ra): 249 (100) M^+ ; 219 (7) $[\text{M}-30]^+$; 203 (43) $[\text{M}-46]^+$; 76 (45) $[\text{M}-173]^+$; 50 (17) $[\text{M}-199]^+$; ^1H NMR (CDCl_3) δ (ppm): 7.35 (ddd, 1H, $J_1=7.76$ Hz, $J_2=7.55$ Hz, $J_3=1.65$ Hz), 7.56 (ddd, 1H, $J_1=7.55$ Hz, $J_2=7.76$ Hz, $J_3=1.38$ Hz), 7.85 (dd, 1H, $J_1=8.12$ Hz, $J_2=1.38$ Hz), 8.08 (dd, 1H, $J_1=7.83$ Hz, $J_2=1.38$ Hz).

2.4.6. Compound 6: 4-iodo-2-nitroaniline

Red solid; mp 103–105°C. IR ν cm^{-1} : 3493.1, 3379.1, (NH_2), 1614.3 (C=C, Ar), 1496.7 and 1335.8 (NO_2); EI-MS 70 eV m/z (% ra): 264 (100) M^+ ; 234 (4) $[\text{M}-30]^+$; 218 (30) $[\text{M}-46]^+$; 91 (29) $[\text{M}-173]^+$; 52 (10) $[\text{M}^+-212]$. ^1H NMR (CDCl_3) δ (ppm): 6.10 (2H, NH_2), 6.60 (d, 1H, $J=8.81$ Hz), 7.56 (dd, 1H, $J_1=1.93$ Hz, $J_2=8.81$ Hz), 8.43 (d, 1H, $J=1.93$ Hz).



Scheme 1. Reaction of anilines with KI/ HNO_3 /bentonite system.



Scheme 2.

3. Results and discussion

The results of the set of experiments carried out with *ortho*, *meta* or *para*-nitroaniline in the presence of KI mixed with the HNO₃/bentonite system (1:10 ratio), are summarized in Scheme 1.

As can be seen, an unusual competitive reaction between nucleophilic (NAS) and electrophilic aromatic substitution (EAS) is detected. The EAS transformation must be achieved by the following oxidation sequence $I^- \rightarrow I^0 \rightarrow I^+$, as demonstrated by the visual detection of molecular iodine during the experimental work.

Another interesting behavior in these reactions, was the absence of nitrating products. This is important because the system HNO₃/bentonite has been used before as nitrating agent for steroid derivatives [11].

For the reaction between *p*-nitroaniline and KI/HNO₃/bentonite a test was run using hydroquinone to probe something about the nature of the reaction. In these conditions, the reaction takes place producing the same reaction products as without the hydroquinone; this result suggests the ionic nature of the NAS and EAS reactions.

Under the presence of KI/HNO₃/bentonite system the *m*-nitroaniline afforded only the NAS product (3); however, the reaction with the *ortho* isomer furnished the 2-nitroiodobenzene (5) by a NAS process as the major product (24%) and only low yield (5%) of the 4-iodo-2-nitroaniline (6) were detected (EAS reaction), this in addition to an unexpected product, the 2, 4-diiodonitrobenzene (4). This molecule must be formed by an EAS over the protonated substrate by means of the Brønsted–Löwry character of the clay, and then by a NAS reaction over the last product (Scheme 2).

Complementarily to the chemical action of the KI/HNO₃/bentonite system, a set of reactions with KI with other oxidizing agents supported on clay, MnO₂/bentonite, Cu(NO₃)₂/bentonite previously used in organic reactions [12,13], and K₂Cr₂O₇/bentonite, or acid systems (HCl/bentonite or H₂SO₄/bentonite) were also tested, and no reaction products were detected. In the same sense, the reactions were performed using KI/HNO₃ without the clay and no reaction products were detected anyhow.

Furthermore, we perform several reactions using NH₄I, NaI, (C₄H₉)₄NI or I₂ and no significative changes were detected, this means that the HNO₃/bentonite acts as acid medium and as oxidizing agent, both necessary for the realized reactions.

Finally, it is worth mentioning that in accordance to a survey on the literature, it seems that there is scarce information about two different reactions catalyzed within one system [14].

4. Conclusions

An interesting example of competitive nucleophilic versus electrophilic aromatic substitution on regioisomeric nitroanilines was detected, using the KI/HNO₃/Bentonite system and microwave radiation in absence of solvent. The behavior of the reactions is defined by the nucleophilic nature of the iodide combined with the action of the clay and to the conversion of the iodide to I⁺ by the HNO₃/Bentonite system.

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