This Accepted Author Manuscript (AAM) is copyrighted and published by Elsevier. It is posted here by agreement between Elsevier and the University of Turin. Changes resulting from the publishing process - such as editing, corrections, structural formatting, and other quality control mechanisms - may not be reflected in this version of the text. The definitive version of the text was subsequently published in *Tetrahedron* 69 (2013) 3212-3217, DOI: 10.1016/j.tet.2013.02.053.

You may download, copy and otherwise use the AAM for non-commercial purposes provided that your license is limited by the following restrictions:

(1) You may use this AAM for non-commercial purposes only under the terms of the CC-BY-NC-ND license.

(2) The integrity of the work and identification of the author, copyright owner, and publisher must be preserved in any copy.

(3) You must attribute this AAM in the following format: Creative Commons BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/deed.en), DOI: 10.1016/j.tet.2013.02.053

Catalytic properties and acidity of 1,2-benzenedisulfonimide and some of its derivatives. An experimental and computational study.

Margherita Barbero, Silvia Berto*, Silvano Cadamuro, Pier Giuseppe Daniele, Stefano Dughera*, Giovanni Ghigo*

Dipartimento di Chimica, Università di Torino, Via P. Giuria 7, 10125 Torino, Italy.

* Corresponding authors:
Tel: +39(11)6705279; Fax: +39(11)6705242; e-mail: silvia.berto@unito.it
Tel: +39(11)6707645; Fax: +39(11)6707642; e-mail: stefano.dughera@unito.it
Tel: +39(11)6707872; Fax: +39(11)6707591; e-mail: giovanni.ghigo@unito.it


Abstract: 1,2-Benzenedisulfonimide (1) has previously been found to be an excellent and, importantly, safe Brønsted acid catalyst. In this work we present the results of a search for derivatives of 1 that are more acidic and effective. Instead of blindly synthesizing a series of analogues, we have carried out a screening process in which the pKₐ of 1 and a set of its derivatives were calculated. The calculated pKₐ values were confirmed experimentally by carrying out determination through potentiometric titrations of some of the compounds: 1, 4-methyl and 4-nitro derivatives of 1. The calculations indicated that the dinitro and 4-nitro derivatives are among the best candidates for the synthesis. The latter was obtained in good yields and tested as a catalyst. Results were excellent as the reactions took place more quickly and at lower temperatures in all cases, and in a number of cases it was even possible to reduce the amount of catalyst.

1. Introduction

We have recently reported on the use of 1,2-benzenedisulfonimide¹ (OBS; 1) in catalytic amounts as a safe, nonvolatile and noncorrosive Brønsted acid in several acid-catalyzed organic reactions that give excellent results.”³
Figure 1. OBS 1.

The catalyst was easily prepared, recovered and purified, ready to be used in further reactions. The high acidity of the Brønsted acid 1 is known in the literature. Hendrickson and coauthors stated that it is fully ionized in water. However, no reliable data has been reported as to its acidity. King and Guo stated that its pKₐ is -4.1 (Hₒ at half-neutralization determined by UV spectra, at 20 °C in H₂O ) but no further details were given; Blaschette, Jones and coauthors reported a value of -1.1 (calculated with the program ACD/pKₐ DB).

In the light of these results, we propose in this work an estimation of the acidity of OBS and some of its derivatives using experimental and theoretical methods. Potentiometric titrations in butanone using picric acid as reference were performed to obtain an acidity scale for these compounds. Moreover, in order to synthesise a derivative that is more acidic than the parent 1 and in order to test and compare it with 1 as a catalyst in some selected reactions, we decided to take advantage of theoretical methods to perform a screening of OBS derivatives based on their pKₐ and therefore single out the most promising derivative for synthesis.

2. Results and discussion

2.1. Theoretical calculation

The calculation of absolute pKₐ of acids is truly a difficult challenge but because our main goal is limited to an estimation of an acidity scale among the set of substituted OBS, we used a different approach. The pKₐ values were obtained as differences (ΔpKₐ) with respect to the pKₐ of the picric acid whose values are available in numerous solvents. With this approach (a sort of “proton-exchange method”) we should have a self-correction of the errors (mainly due to the continuum method used to include the solvent effects) that should be particularly efficient when comparing OBS and its derivatives. The ΔpKₐ values were calculated using the equilibrium shown in Scheme 1.
Scheme 1. Equilibrium between picric acid and 1

The $\Delta pK_a^A$ is then easily calculated as:

$$\Delta G = \frac{\Delta pK_a^A}{2.303 \, RT}$$

where $\Delta G$ is the free energy of the above equilibrium, R the gas constant and T the temperature (25 °C).

Before proceeding with the calculation of the p$K_a$ of 1, we tested the computational approach (see section 4.6) and calculated a selected number of p$K_a$ values for which the experimental values are available. These includes phenols, sulfonic acids and sulfonimides (see Supporting Information, Table 1). The accuracy ($\Delta pK_a = \pm 1$) was satisfactory.

The effect of six different substituents (mostly electron-withdrawing) on 1 p$K_a$ in butanone was calculated. Table 1 shows the $\Delta G$ of the above equilibrium, the $\Delta pK_a$ with respect to the picric acid ($\Delta pK_a^A$) and with respect to the unsubstituted OBS ($\Delta pK_a^O$). $\Delta pK_a^A$ is then used to calculate the absolute p$K_a$ of 1 using the known the p$K_a$ of picric acid (8.2). The last column reports the experimental value (see section 2.3). The error in the calculated $\Delta pK_a^O$ (0.2) is below the experimental error.

Table 1. Calculated ($pK_a^{calc}$) and experimental ($pK_a^{exp}$) acidity constants in butanone.

<table>
<thead>
<tr>
<th>1,2-benzenedisulfonimide</th>
<th>$\Delta G$</th>
<th>$\Delta pK_a^A$</th>
<th>$\Delta pK_a^O$</th>
<th>$pK_a^{calc}$</th>
<th>$pK_a^{exp}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image.png" alt="Diagram" /></td>
<td>-3.2</td>
<td>-2.3</td>
<td>-</td>
<td>5.9</td>
<td>6.09 ± 0.04</td>
</tr>
<tr>
<td><img src="image.png" alt="Diagram" /></td>
<td>-6.1</td>
<td>-4.5</td>
<td>-2.1</td>
<td>3.7</td>
<td>N/A</td>
</tr>
<tr>
<td>Compound</td>
<td>ΔpKₐ/O</td>
<td>ΔpKₐ</td>
<td>ΔpKₐ</td>
<td>ΔpKₐ</td>
<td>ΔpKₐ</td>
</tr>
<tr>
<td>------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>O₂N-SO₃</td>
<td>-5.9</td>
<td>-4.4</td>
<td>-2.0</td>
<td>3.8</td>
<td>4.3 ± 0.04⁹</td>
</tr>
<tr>
<td>Me-SO₃</td>
<td>-2.6</td>
<td>-1.9</td>
<td>+0.5</td>
<td>6.3</td>
<td>6.81 ± 0.01⁹</td>
</tr>
<tr>
<td>F₂C-SO₃</td>
<td>-5.7</td>
<td>-4.2</td>
<td>-1.8</td>
<td>4.0</td>
<td>N/A</td>
</tr>
<tr>
<td>NC-SO₃</td>
<td>-6.4</td>
<td>-4.7</td>
<td>-2.4</td>
<td>3.5</td>
<td>N/A</td>
</tr>
<tr>
<td>MeO₂S-SO₃</td>
<td>-5.8</td>
<td>-4.3</td>
<td>-1.9</td>
<td>3.9</td>
<td>N/A</td>
</tr>
<tr>
<td>O₂N-SO₃</td>
<td>-9.8</td>
<td>-7.2</td>
<td>-4.9</td>
<td>1.0</td>
<td>N/A</td>
</tr>
<tr>
<td>O₂N-SO₃</td>
<td>-10.0</td>
<td>-7.3</td>
<td>-5.0</td>
<td>0.9</td>
<td>N/A</td>
</tr>
</tbody>
</table>

⁹ Kcal mol⁻¹.

⁸ Values obtained using the potentiometric method, at T = 25°C.

⁹ Standard deviation.

Not surprisingly, the electron withdrawing groups increase acidity by a factor of 100 (ΔpKₐ/O ~ -2) for the monosubstituted and by a factor of 10000 (ΔpKₐ/O ~ -5) for disubstituted ones. The electronic effects (whether electron donor or electron withdrawing) are hardly dependent on the position of the substituent, and they are almost the same in the acid as in its anion conjugated base (see the group charges in Table 2 of Supporting Information). With the deprotonation of the acid, substituent group charge is reduced (made more negative or less positive) by 0.02 electrons in all cases (for each substituent), testifying that there is no direct effect on the negative charge in the conjugated base. This can also be seen in Figure 2, which shows the highest occupied molecular orbital (HOMO) of the anion of 3,5-dinitrobenzenedisulfonimide. This orbital gives a rough picture of the negative charge distribution and we can see that the nitro groups are not involved.
**Figure 2.** HOMO in 3,5-dinitrobenzenedisulfonimide anion.

### 2.2 Preparation of 1,2-benzenedisulfonimides 5

We synthesized two derivatives of 1, one with an electron withdrawing group, 4-nitro-1,2-benzenedisulfonimide (5a) and the other with an electron donating group, 4-methyl-1,2-benzenedisulfonimide (5b). First of all, the pKₐ values of 5a and 5b were measured experimentally. Then, the more acidic 5a (compared to parent 1) was tested as catalyst in some selected reactions. Compounds 5a and 5b were prepared using the same protocol as previously reported, starting from anthranilic acids 2a and 2b (Scheme 2).

![Scheme 2](image)

**Scheme 2.** Preparation of derivatives of OBS 5a, b.

The yields of the intermediates 3a and 3b, 4a and 4b and of the imides 5a and 5b are reported in Table 2.
**Table 2.** Synthetic sequence for 1,2-benzenedisulfonimides 5a, b.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>Products and Yields(^a) (%)</th>
<th>Products and Yields(^a) (%)</th>
<th>Products and Yields(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>3a, 62</td>
<td>4a, 91</td>
<td>5a, 94</td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>3b, 88</td>
<td>4b, 95</td>
<td>5b, 95</td>
</tr>
</tbody>
</table>

\(^a\) Yields refer to the pure and isolated products

Unfortunately, the attempts to prepare 3,5-dinitro-1,2-benzenedisulfonimide (5c, a compound which would be more acidic than 5a from a theoretical point of view) failed. In fact, it was impossible to obtain intermediate 3c from anthranilic acid 2c (prepared as reported in the literature \(^9\)) using the standard reaction conditions. Moreover, it must be stressed that the reaction became more difficult even with only one nitro group. In fact, an internal diazonium salt is the key intermediate in the first step (Scheme 1). The presence of a single electron-withdrawing group probably already makes the diazotization reaction more difficult (the yield of 3a is lower than that of 3b), and the presence of two completely prevented it and only unreacted 2c was recovered at the end of the reaction. It should also be noted that the direct nitration of the intermediates 3a, 4a or 5a also failed

2.3. **Measurement of pK\(_a\) of 1,2-benzenedisulfonimides 1, 5a, 5b.**

As reported by Kütt, Koppel, Leito and coauthors,\(^7\) the acidity measurements of acid molecules turns out to be a useful tool in the design and use of these compounds. However, the choice of a measurement medium in which to obtain the acid strength of a strong acid is no simple matter. Typical solvents (e.g. heptane, DMSO, MeCN) are not convenient for studying strong acids, because of their low polarity, poor ion solvating ability or simply because they are too basic. We found that butanone is a good solvent; potentiometric titrations in butanone allowed us to differentiate the 1,2-benzenedisulfonimides on the basis of their acid properties. In fact, the large potential range available in butanone affords a useful scale for the potentiometric determination of relative acidity and makes it possible to differentiate strong acids.

Using the method described in the experimental section,\(^8\) it was possible to build a self-consistent acidity scale which was anchored to the pK\(_a\) of picric acid using potentiometric apparatus. The pK\(_a\) values of compounds 1, 5a and 5b were measured and are reported in Table 1. For the first time, an experimental estimation of the acidity of these compounds is obtained and the results are those expected based on the characteristics of the derivative and are in good accordance with those obtained by theoretical calculations.
2.4. 4-Nitro-1,2-benzenedisulfonimide (5a) as a catalyst.

We have recently reported the use of 1,2-benzenedisulfonimide (1, Figure 1) in catalytic amounts as a safe, nonvolatile and noncorrosive Brønsted acid in some acid-catalyzed organic reactions such as etherification,\(^{14}\) esterification,\(^{15,16}\) acetalization,\(^{16}\) the Ritter reaction,\(^{17}\) the Nazarov electrocyclization,\(^{18}\) the disproportionation of dialkyl diarylmethyl ethers,\(^{19}\) the Hosomi-Sakurai reaction,\(^{20}\) the Friedländer annulation,\(^{21}\) the Pictet-Spengler reaction,\(^{22}\) the Mukaiyama-aldol reaction,\(^{23}\) preparation of triaryl and trisindolylmethanes \(^{24}\) and the Strecker reaction.\(^2\)

In general, all synthetic methods require mild reaction conditions and short reaction times. It is worth noting that good selectivity and the absence or minimal formation of by-products was observed in all cases. Moreover, 1 can easily recovered from the reaction mixtures in high yield.

In the light of these results, we decided to test 5a as a catalyst in various selected reactions in order to compare its catalytic activity with the already known activity of 1.

First of all, we examined the esterification reaction between phenyl acetic acid and butan-1-ol.

As reported by us,\(^3\) the reaction catalyzed by 1, using toluene as a solvent, required the presence of 25 mol-% of catalyst. It was completed after heating at 90 °C for 1.5 hours. The yield of butyl phenylacetate was 90% (Table 3, entry 1).

**Table 3.** Selected reaction catalyzed by 5a.

| Entry | Reaction and references | Catalysts (mol-\%) | Temp (°C) | Time (h) | Yields (%)
|-------|-------------------------|-------------------|-----------|----------|-----------
| 1     | BnCOOH + n-BuOH → BnCOOBu-n | 1 (25)           | 90        | 1.5      | 90\(^{bc}\) |
|       |                          | 5a (5)           | r.t.      | 3        | 87\(^{bc}\) |
| 2     | COOH + n-BuOH → COOBu-n   | 1 (20)           | 90        | 24       | 37\(^{bc}\) |
|       |                          | 5a (10)          | 90        | 5        | 84\(^{bc}\) |
| 3     | OH + MeCN → NHCOMe       | 1 (10)           | 82        | 8        | 89\(^d\)   |
|       |                          | 5a (10)          | 82        | 3        | 91\(^d\)   |
| 4     | t-BuOH + MeCN → t-BuNHCOMe | 1 (20)           | 82        | 72       | 83\(^d\)   |
|       |                          | 5a (20)          | 82        | 24       | 87\(^d\)   |
| 5     | OMe + TMS → OMe          | 1 (5)            | 45        | 2        | 90\(^{ef}\) |
|       |                          | 5a (5)           | r.t.      | 1        | 92\(^{ef}\) |
6

\[
\text{OH} \quad \text{Me} \quad + \quad \text{CH}_2\text{SiMe}_3 \quad \rightarrow \quad \text{H} \quad \text{Me}
\]

**1** (30) 70 24  72\(^{h,g}\)

**5a** (10) 80 12  82\(^{f,g}\)

7

\[
\text{O} \quad \text{NH}_2 \quad + \quad \text{O} \quad \rightarrow \quad \text{O} \quad \text{Me} \quad \text{Me}
\]

**1** (10) 80 28  90\(^{h,f}\)

**5a** (5) 80 12  85\(^{h,f}\)

8

\[
\text{O} \quad \text{NH}_2 \quad + \quad \text{O} \quad \rightarrow \quad \text{O} \quad \text{Me} \quad \text{Me}
\]

**1** (5) 80 4  90\(^{h,f}\)

**5a** (5) 50 2  86\(^{h,f}\)

9

\[
\text{MeO} \quad \text{C} \quad \text{H} \quad \text{CHO} \quad \rightarrow \quad \text{MeO} \quad \text{C} \quad \text{H}
\]

**1** (10) 80 6  89\(^{f,h}\)

**5a** (5) 80 2  92\(^{f,h}\)

10

\[
\text{MeO} \quad \text{OH} \quad + \quad \text{OH} \quad \rightarrow \quad \text{MeO} \quad \text{OH}
\]

**1** (5) 80 3  100\(^{b,f}\)

**5a** (5) r.t. 3  100\(^{b,f}\)

\(^{a}\) Yields refer to the pure and isolated products. The physical and spectroscopic data of the obtained products are in accordance with those previously reported by us.

\(^{b}\) The reactant ratio was 1: 1.1.

\(^{c}\) The solvent was toluene.

\(^{d}\) MeCN was the reactant and the solvent.

\(^{e}\) The reactant ratio was 1: 1.2.

\(^{f}\) The reaction was carried out in neat conditions.

\(^{g}\) The reactant ratio was 1: 1.5.

\(^{h}\) The reactants was in equimolar amount.

Interestingly, the reaction took place at room temperature in the presence of only 5 mol-% of **5a** as a catalyst and a good yield (87%) of butyl phenylacetate was obtained nonetheless (Table 3, entry 1). The catalyst **5a** was easy recovered (90%) by simply evaporating the aqueous layer at reduced pressure.

On the basis of this excellent result, **5a** was used as the catalyst in nine other reactions that had previously been performed by us in the presence of **1**. Table 3 shows the results.

It can be stated that **5a** is more effective than **1**. In general, the reactions took place more quickly and at lower temperatures. Moreover, in some cases, a smaller amount of catalyst was needed.
(Table 2; entries 2, 6, 7, 9). The yields of the target products were very similar to those obtained using 1, with the sole exception of entry 2, where a sharp increase in yield was observed.

It can be stated that 5a is more effective than 1. In general, the reactions took place more quickly and at lower temperatures. Moreover, in some cases, a smaller amount of catalyst was needed.

(Table 2; entries 2, 6, 7, 9). The yields of the target products were very similar to those obtained using 1, with the sole exception of entry 2, where a sharp increase in yield was observed.

3. Conclusions

The theoretical approach allowed us to calculate the pH of OBS (1) and a set of its derivatives. The calculated values were confirmed by experimental determination using potentiometric titrations on some of the species; 1, 5a and 5b. The calculations also suggested which derivatives were the best candidates for synthesis. Of them, 5a was obtained in a good yield and was tested as a catalyst in ten selected reactions, obtaining generally better results than those obtained with 1.

4. Experimental section

4.1. General

Analytical grade reagents and solvents were used and reactions were monitored, where possible, by GC, GC-MS and TLC. Column chromatography and TLC were performed on a Merck silica gel 60 (70-230 mesh ASTM) and GF 254, respectively. Petroleum ether (PE) refers to the fraction boiling in the range 40–70 °C. Room temperature is 20–25 °C. Mass spectra were recorded on an HP 5989B mass selective detector connected to an HP 5890 GC, cross-linked methyl silicone capillary column. 1H NMR and 13C NMR spectra were recorded on a Bruker Avance 200 spectrometer at 200 and 50 MHz respectively. IR spectra were recorded on a Perkin Elmer Spectrum BX FT-IR spectrometer as solutions in CHCl3. Potentiometric measurements were performed using a Metrohm mod. 713 potentiometer (resolution of ±0.1 mV) coupled with a Metrohm 665 Dosimat burette (minimum volume deliverable of ±0.001 cm3) and equipped with a Metrohm combined glass electrode suitable for measurements in non aqueous solutions (Solvotrode mod. 6.0229.100). The potentiometric titrations were carried out in a stream of anhydrous nitrogen gently bubbled in the titration cell to avoid O2 and CO2 contamination. The measurement cells were thermostated at (25±0.1 ºC) by means of a water circulation from a thermocryostat (mod. D1-G Haake).

5-Nitroantranilic acid, 5-methylantranilic acid, benzoic acid, calcium sulfate dihydrate, picric acid, butanone and tetrabutylammonium hydroxide 0.1 mol/l standard solution in 2-propanol/methanol were purchased from Sigma-Aldrich. Thymol blue indicator was a Fluka
product. OBS (1) and 3,5-dinitroanilinic acid were prepared as reported in the literature. Calcium sulfate dihydrate is dried at 240°C for 10-12 hours in order to obtain the anhydrous form. The structures and purity of all the products obtained in this work were confirmed by their spectroscopic (NMR, MS and IR) data. Satisfactory microanalyses were obtained for all the new compounds.

4.2. 2-(3-Methylbutoxy)-1,3-benzodithioles 3. General procedure

As reported by us, 3-methylbutyl nitrite (2.4 mmol, 0.28 g), 3-methylbutan-1-ol (2 mmol, 0.18 g) and CS₂ (16.6 mmol, 1.26 g) were dissolved in 1,2-dichloroethane (15 mL) and heated to reflux at 82 °C. Anthranilic acid 2 (2 mmol) dissolved in 1,4-dioxane (6 mL) was added dropwise to the previously prepared mixture. The resulting mixture was initially stirred at reflux for 45 min and then at room temperature for 1 h. For the preparation of 3a, it was necessary to stir at reflux for 3.5 h. The reaction mixture was poured into Et₂O–H₂O (100 mL, 1:1). The aqueous layer was separated and extracted with Et₂O (2 × 50 mL). The combined organic extracts were washed with H₂O (2 × 50 mL) and a saturated solution of Na₂CO₃ (50 mL), dried over Na₂SO₄ and evaporated under reduced pressure. The crude residue, purified by column chromatography (PE–Et₂O 95:5), afforded the pure title compound 3.

4.2.1. 5-Nitro-2-(3-methylbutoxy)-1,3-benzodithiole (3a). Yellow solid; 0.35 g (yield: 62%); mp 69–70 °C (EtOH); Rf = 0.70. IR (CHCl₃) ν (cm⁻¹): 3176, 2963, 1815, 1785, 1690, 1560, 1378, 1210, 1100, 795. ¹H NMR (200 MHz, CDCl₃): δ [8.14 (d, J = 2.0 Hz, 1H), 7.90 (dd, J₁ = 8.2 Hz, J₂ = 2.0 Hz, 1H), 7.39 (d, J = 8.2 Hz, 1H), 6.85 (s, 1H), 3.37 (t, J = 6.2 Hz, 2H), 1.66–1.50 (m, 1H), 1.40–1.31 (m, 2H), 0.81 (d, J = 6.2 Hz, 6H); ¹³C NMR (50 MHz, CDCl₃): δ 145.7, 144.9, 138.3, 125.7, 121.4, 120.5, 91.1, 63.2, 37.4, 24.8, 22.3; calcd for C₁₂H₁₅NO₃S₂: C 50.51%; H 5.30%; N 4.91%; S 22.47%; found: C 50.47%; H 5.38%; N 4.89% S 22.52%.

4.2.2. 5-Methyl-2-(3-methylbutoxy)-1,3-benzodithiole (3b). Viscous yellow oil; 0.45 g (yield: 88%); Rf = 0.80. IR (CHCl₃) ν (cm⁻¹): 3160, 2988, 2247, 1820, 1770, 1630, 1390, 1210, 1084, 800 ¹H NMR (200 MHz, CDCl₃): δ [7.18–7.11 (m, 2H), 6.85 (d, J = 8.2 Hz, 1H), 6.70 (s, 1H), 3.37 (t, J = 6.2 Hz, 2H), 2.24 (s, 3H), 1.64–1.49 (m, 1H), 1.35–1.29 (m, 2H), 0.80 (d, J = 6.2 Hz, 6H); ¹³C NMR (50 MHz, CDCl₃): δ 142.0, 135.5, 133.0, 126.5, 122.6, 121.7, 90.3, 62.8, 37.9, 25.0, 22.6; MS (m/z, EI) = 254 (M⁺); calcd for C₁₃H₁₈OS₂: C 61.38%; H 7.13%; S 25.20%; found: C 61.41%; H 7.18 %; S 25.21%.

4.3. 1,2-Benzenedisulfonyl chlorides 4. General procedure
As reported by us, 1,3-benzodithiole 3 (2 mmol) was dissolved in tert-butyl alcohol (10 mL), CH₂Cl₂ (8 mL) and H₂O (1.5 mL). The resulting mixture was cooled to 0-5 °C. Chlorine was bubbled through while the temperature was maintained at 0-5 °C and the reaction mixture vigorously stirred. The reaction was monitored using TLC (PE-EtOAc 7: 3). After 1 h, the reaction was complete when the spot of 3 disappeared and there was only one other spot. The reaction mixture was poured into CH₂Cl₂–H₂O (100 mL, 1:1) The aqueous layer was separated and extracted with CH₂Cl₂ (2 [×] 50 mL). The combined organic extracts were washed with a 5% NaOH solution (2 [×] 50 mL), dried over Na₂SO₄ and evaporated under reduced pressure. The crude residue was the pure title compound 4.

4.3.1. 4-Nitro-1,2-benzenedisulfonyl chloride (4a). Yellow solid; 0.58 g (yield: 91%); mp 244 °C (EtOH); R₇ = 0.31. IR (CHCl₃) ν (cm⁻¹): 3015, 1590, 1355, 1220, 1190, 800. ¹H NMR (200 MHz, CDCl₃): δ 9.07 (d, J = 2.0 Hz, 1H), 8.75 (dd, J₁ = 8.2 Hz, J₂ = 2.0 Hz, 1H), 8.61 (d, J = 8.2 Hz, 1H)., ¹³C NMR (50 MHz, CDCl₃): δ 150.6, 144.5, 142.7, 134.0, 130.1, 127.2; calcd for C₆H₆Cl₂NO₆S₂: C 22.51%; H 0.94%; Cl 22.15%; N 4.38%; S 20.03%; found: C 22.53%; H 0.90%; Cl 22.55%; N 4.42%; S 16.95%.

4.3.2. 4-Methyl-1,2-benzenedisulfonyl chloride (4b). White solid; 0.55 g (yield: 95%); mp 106–107 °C (EtOH); R₇ = 0.38. IR (CHCl₃) ν (cm⁻¹): 3033, 3010, 1340, 1212, 1200, 814 ¹H NMR (200 MHz, CDCl₃): δ 8.26 (d, J = 8.2 Hz, 1H), 8.17 (d, J = 2.0 Hz, 1H), 7.72 (dd, J₁ = 8.2 Hz, J₂ = 2.0 Hz, 1H), 2.57 (s, 3H); ¹³C NMR (50 MHz, CDCl₃): δ 148.7, 142.3, 139.4, 136.3, 132.9, 132.6, 21.8; calcd for C₇H₇Cl₂O₄S₂: C 29.08%; H 2.09%; Cl 24.52%; S 22.18%; found: C 29.03%; H 2.12%; Cl 24.60%; S 22.25%.

4.4. 1,2-Benzenedisulfonimides 5. General procedure

As reported by us, 1,2-benzenedisulfonyl chloride 4 (2 mmol) was dissolved in toluene (8 mL) and EtOH (12 mL). The resulting mixture was cooled to 0-5 °C. Ammonia was bubbled through while the temperature was maintained at 0-5 °C and the reaction mixture vigorously stirred. The reaction was monitored by TLC (PE–EtOAc 7: 3). After 30 min, the reaction was complete when the spot of 4 disappeared. The mixture was first filtered in order to eliminate NH₄Cl and then the solvent was evaporated under reduced pressure. The crude residue was dissolved in H₂O and passed through a Dowex (HCR–W2) column (H₂O) to afford the pure title compound 5.
4.4.1. 4-Nitro-1,2-benzenedisulfonimide (5a). Brown solid; 0.50 g (yield: 94%); mp 160–161 °C (EtOH); IR (CHCl₃) ν (cm⁻¹): 3500, 3015, 1630, 1590, 1385, 1218, 818. ¹H NMR (200 MHz, MeOH-d₄): δ 8.74 (d, J = 2.0 Hz, 1H), 8.69 (dd, J₁ = 8.2 Hz, J₂ = 2.0 Hz, 1H) 8.14 (d, J = 8.2 Hz, 1H); ¹³C NMR (50 MHz, MeOH-d₄): δ 154.8, 141.8, 137.0, 128.1, 122.8, 116.9; calcd for C₆H₄N₂O₆S₂: C 27.27%; H 1.53%; N 10.60%; S 24.27%; found: C 27.32%; H 1.49%; N 10.67%; S 24.21%.

4.4.2. 4-Methyl-1,2-benzenedisulfonimide (5b). Pale brown solid; 0.44 g (yield: 95%); mp 121–122 °C (EtOH); IR (CHCl₃) ν (cm⁻¹): 3450, 3027, 1625, 1400, 1320, 1235, 810; ¹H NMR (200 MHz, MeOH-d₄): δ 7.77 (d, J = 8.2 Hz, 1H), 7.68 (s, 1H) 7.62 (d, J = 8.2 Hz, 1H), 2.51 (s, 3H); ¹³C NMR (50 MHz, MeOH-d₄): δ 145.2, 141.8, 138.5, 134.2, 121.7, 121.0, 20.3; calcd for C₇H₇N₂O₄S₂: C 36.04%; H 3.02%; N 6.00%; S 27.49%; found: C 36.08%; H 3.05%; N 5.97%; S 27.52%.

4.5 Potentiometric measurements

Solutions of compounds 1, 5a, 5b and picric acid (2·10⁻³ mol/l) in butanone were titrated with tetrabutylammonium hydroxyde 0.1 mol/l standard solution. Each titration was repeated in triplicate. All titrations were carried out with about 2 g of anhydrous calcium sulfate dispersed in the solution in order to avoid water contamination. Under these conditions a good stability of potentials was obtained. The concentration of the tetrabutylammonium hydroxide standard solution was controlled by weekly visual titrations of benzoic acid solutions and thymol blue as indicator.
The pKₐ of picric acid obtained by Norberg in butanone (Kₐ = 6.4·10⁻⁹)²² was taken as a reference. The pKₐ of compounds 1, 5a and 5b were then calculated with the equation 1, derived from the Henderson-Hasselbalch equation, using the difference between the half-neutralization potentials measured for OBS and picric acid solutions, assuming that, in the same experimental conditions, the formal potential of the glass electrode is the same for the two solutions. In order to assure that the electrode performance were the same for the reference and the benzenedisulfonimide, the titration of picric acid is performed before each titration of 1, 5a and 5b solutions.

\[ pK_{OBS}^{OBS} = pK_{OBS}^{PA} + \frac{E_{PA}^{1/2} - E_{OBS}^{1/2}}{59.16} \]  

The \( E_{PA}^{1/2} \) and \( E_{OBS}^{1/2} \) are the half-neutralization potentials (mV) measured for picric acid (PA) and OBS (1) solutions respectively; \( pK_{OBS}^{PA} \) and \( pK_{OBS}^{OBS} \) are the acidic constants of PA and OBS, and 59.16 mV is the Nernstian slope.

The ΔpKₐ between the picric acid and the studied compounds correspond to the chemical equilibrium reported in the paragraph 2.1.

4.6 Computational method

All structures (acids and conjugated anion bases) were optimized using the density functional method (DFT)²⁴ with the recently developed functional M06-2X²⁵ with the 6-31+G(d,p)²⁶,²⁷ basis set, and using vibrational analysis to check the nature of the critical points²⁷ (all data are reported in the Supporting Information). The energy values were then refined using single-point calculations with the basis set 6-311+G(3df,2p)²⁸,²⁹ and combined with the thermal corrections obtained with the smaller basis set to give free energy values. Solvent effects were introduced both in geometry optimization and single point calculations using the Polarized Continuum Method (IEF-PCM)²⁰ within the universal Solvation Model Density (SMD).²⁰ Calculations were performed by the quantum package Gaussian 09-A.02.²⁰ Figure 2 was obtained using the graphical program Molden.²⁰

Acknowledgments

This work was supported by the University of Torino.

Supplementary data

1
Supplementary data associated with this article can be found in the online version at doi...:
Total (in au) and relative (in kcal mol\(^{-1}\)) electronic energies and free energy corrections are reported.
Nuclear coordinates (in Ångstrom) follows.

References


Graphical Abstract

Catalytic properties and acidity of benzenedisulfonimide and some derivatives. An experimental and theoretical study.