

o-Benzenedisulfonimide: A Novel and Reusable Catalyst for Acid-Catalyzed Organic Reactions

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Abstract: The *o*-benzenedisulfonimide is used as Brønsted acid in catalytic amounts in various acid-catalyzed organic reactions, such as etherification, esterification, and acetalization; the conditions required are mild and in the considered examples the results are always good. A useful aspect of the use of this catalyst is its easy recovery in high yield from the reaction mixture and its reuse in other reactions, with economic and ecological advantages.

Key words: *o*-Benzenedisulfonimide, Brønsted acid, acid-catalyzed organic reactions, reusable catalyst, dehydrative reactions

The *o*-benzenedisulfonimide (**1**) was first reported in 1921 and 1926 by Holleman¹ and by Hurlley and Smiles,² respectively, and more recently by Hendrickson,³ Blaschette,⁴ Davis,⁵ and their co-workers. The key intermediate is the *o*-benzenedisulfonyl chloride, which can be prepared starting from the commercially available *o*-benzenedisulfonic acid dipotassium salt,^{2,5} anthranilic acid,⁶ *o*-aminobenzenesulfonic acid,⁷ and *o*-bis(methylthio)benzene;⁸ now it is also commercially available by many suppliers.

In the last decade, we reported our results on the synthetic applications of the *N*-hydroxy derivative of **1** and of its conjugate base as stabilizing counterion for arenediazonium *o*-benzenedisulfonimides, a new family of arenediazonium salts, exceptionally stable in the dry state and therefore good synthesis intermediates both in aqueous and in anhydrous conditions.⁹

Recently, in the course of our investigations concerning the reactivity of these salts in metal-catalyzed cross-coupling reactions,¹⁰ we studied the Heck-type arylation of allylic alcohols.^{10c} Along with the expected mixtures of β - and α -arylated carbonyl compounds and of arylated allylic alcohols, in some cases we isolated the ethoxy derivatives **2** (Figure 1), whose formation was ascribed to a Tsuji–Trost reaction of the solvent ethanol on the intermediate arylated allylic alcohol.¹¹

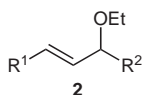


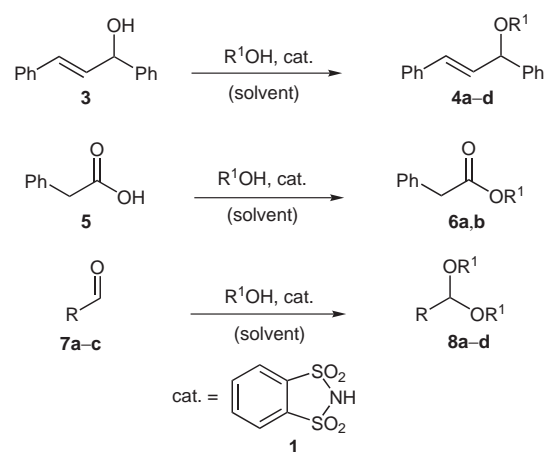
Figure 1

Initially, to confirm this hypothesis, we reacted the allylic alcohol 1,3-diphenylprop-2-en-1-ol (**3**) in EtOH, in the presence of Pd(OAc)₂ as precatalyst, but surprisingly we did not observe the formation of the corresponding ethoxy derivative. Instead, the reaction occurred in the absence of the metal catalyst, but in the presence of catalytic amounts of **1**.

The high acidity of this Brønsted acid is known,¹² but to the best of our knowledge, for the first time this strong acid is shown to effect a dehydration of an alcohol, namely the allylic alcohol **3**, to give in ethanol the isolated ethyl ether. As a consequence, we decided to evaluate the synthetic potential of the imide **1** as a novel Brønsted acid catalyst in some acid-catalyzed reactions, frequently used in organic synthesis to introduce useful protecting groups.

A further valuable aspect of the use of **1** is its easy recovery in high yield from the reaction mixture, due to its complete solubility in water, and its reuse without loss of catalytic activity in other reactions, with economic and ecological advantages.

In this paper we describe our preliminary results obtained in some explorative acid-catalyzed reactions,¹³ carried out in the presence of catalytic amounts of **1** (Scheme 1).



Scheme 1

Etherification, esterification, and acetalization were chosen in view of the synthetic significance and simplicity of the dehydrative acid-catalyzed methods of synthesis.^{14–16}

In Table 1 we report detailed descriptions of the examined reactions (reactants, molar ratio, reaction conditions) and results (yields of pure isolated products by flash chromatography).

All the considered reactions were conducted in an open-air flask, using analytical grade reagents and solvents; water is the only side product.

The etherification of 1,3-diphenylprop-2-en-1-ol (**3**) with primary or secondary alcohols (entries 1–4) occurred in very mild conditions (r.t. or 60 °C) and high yields. The reaction was carried out in excess of aliphatic alcohol as solvent (entries 1 and 2) or in etherate solvent with the alcohols in stoichiometric amounts or in slight excess (THF; entries 3 and 4). In the course of the reactions we observed the exclusive formation of the mixed ethers **4a–d**; no traces were detected or isolated of the symmetric ethers.

The preferred catalytic amount of *o*-benzenedisulfonimide (**1**) was 5% mol (increasing amount gave yields slightly better; entries 1–3, values in parentheses).¹⁷

Direct dehydrative esterification of phenylacetic acid (**5**) with primary aliphatic alcohols was achieved in high yields and purity, by carrying out the reaction in toluene at 90 °C, with the reagents in almost equimolar amounts and in the presence of 20–25% mol of *o*-benzenedisulfonimide (**1**).¹⁸

Finally, to further explore the synthetic usefulness of the *o*-benzenedisulfonimide as acid catalyst, we prepared some dimethyl acetals in mild reaction conditions (at r.t. and in air) and short times. Good conversions were obtained for the aromatic aldehyde **7a** (entry 7), the conjugated cinnamic aldehyde (**7b**, entry 8), and the acid-sensitive aldehyde **7c** (entry 9). The acetal formation was

Table 1 *o*-Benzenedisulfonimide-Catalyzed Etherification, Esterification, and Acetalization Reactions

Entry	Reactants 3, 5, 7	R ¹ OH	Reactants (molar ratio)	1 (mol%)	Solvent	Temp (°C)	Time (min)	Products 4, 6, 8	Yield (%) ^{a,b}
1		EtOH		5	EtOH	r.t.	120		77 (81) ^c
2	3	<i>i</i> -PrOH		5	<i>i</i> -PrOH	r.t.	15		74 (77) ^c
3	3	BnOH	1:1	5	THF	r.t.	60		85 (90) ^c
4	3	BuOH	1:2	5	THF	Reflux	150		70
5	PhCH ₂ COOH 5	BuOH	1:1.1	25	PhMe	90	90	PhCH ₂ COO <i>n</i> -Bu 6a	90
6	5	<i>n</i> -C ₈ H ₁₇ OH	1:1	20	PhMe	90	90	PhCH ₂ COO <i>n</i> -C ₈ H ₁₇ 6b	85
7	4-ClC ₆ H ₄ CHO 7a	MeOH		0.5	MeOH	r.t.	10	4-ClC ₆ H ₄ CH(OMe) ₂ 8a	85 (90) ^d
8	PhCH=CHCHO 7b	MeOH		0.5	MeOH	r.t.	10	PhCH=CHCH(OMe) ₂ 8b	64 (72) ^{d,e}
9		MeOH		0.5	MeOH	r.t.	10		64 (65) ^{d,e}
10	7a	HOCH ₂ CH ₂ OH 9	1:3	1	PhMe	90	60		87 ^c

^a Yields refer to pure isolated products (flash chromatography).

^b Products were characterized by GC-MS, ¹H NMR, and ¹³C NMR spectra and by comparison with known or authentic commercial compounds.

^c In parentheses yield of product obtained in the presence of **1** 10% mol.

^d In parentheses yield of product obtained in the presence of **1** 1% mol.

^e Unreacted carbonyl compound **7** was recovered (entry 8: **7b**, 23%; entry 9: **7c**, 5%; entry 10: **7a**, 11%).

also achieved in solvent (molar ratio **7a**:ethane-1,2-diol (**9**) = 1:3, in toluene at 90 °C; entry 10). The optimal catalytic amount of catalyst **1** was 0.5–1% mol, neutralized at the end of the reaction by addition of solid NaHCO₃; pure acetals were isolated by flash chromatography on silica gel deactivated by Et₃N.¹⁹

From all the reactions, after the workup of the reaction mixture, o-benzenedisulfonimide (**1**) was recovered in high yield, recyclable as catalyst for other reactions.²⁰

Amongst the examples reported in Table 1 and taking into consideration only Brønsted acid catalyzed dehydrative syntheses, ether **4c** was prepared in 77% yield from the starting alcohols in the presence of Ir complex activated by H₂ molecule;²¹ esters **6a** and **6b** were prepared from acid **5** and the corresponding alcohols in comparable yields by prolonged heating at higher temperatures;²² acetals **8a,b,d** were obtained directly from the corresponding aldehydes and alcohols in comparable yields, but after longer reaction times.²³

The advantages of the proposed methodology are mild reaction conditions, short reaction times, and no formation of side products. Compared to strong liquid or solid Brønsted acids, extensively used from research laboratories to chemical manufacturing plants, the here proposed catalyst turns out to be a nontoxic, nonvolatile and non-corrosive chemical product, easily recoverable from the reaction mixture without need of binding to solid matrix. A thorough study on its wider use in organic transformations is in progress.

In this communication, we reported the synthetic applicability of the o-benzenedisulfonimide as a novel acid catalyst for acid-catalyzed organic reactions, in view of the continuous interest in new methods of homogeneous catalysis, environmentally friendly, and economically sustainable.

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(17) **Typical Procedure for *o*-Benzenedisulfonimide-Catalyzed Etherification (Entry 1, Table 1)**

To a solution of 1,3-diphenylprop-2-en-1-ol (**3**; 0.42 g, 2.0 mmol) in abs. EtOH (10 mL) was added *o*-benzenedisulfonimide (**1**; 5 mol%; 0.02 g, 0.1 mmol); the reaction mixture was stirred at r.t. The reaction was monitored by TLC (PE–Et₂O, 6:4), GC, and GC-MS analyses until complete disappearance of the starting material. Then the reaction mixture was evaporated under reduced pressure and the residue was poured into Et₂O–H₂O (40 mL, 1:1). The aqueous layer was separated. The organic extract was washed with H₂O (20 mL), dried over Na₂SO₄, and evaporated under reduced pressure. The crude residue was chromatographed on a short column (PE–Et₂O, 6:4) to provide pure (*E*)-1,3-diphenyl-3-ethoxyprop-1-ene (**4a**; GC, GC-MS, TLC, ¹H NMR) in 77% yield (0.37 g); colorless oil. ¹H NMR: δ = 1.33 (t, *J* = 7.0 Hz, 3 H), 3.60 (superimposed q, *J* = 7.0 Hz, 2 H diastereotopic), 4.98 (d, *J* = 6.8 Hz, 1 H), 6.38 (dd, *J* = 16.0, 6.8 Hz, 1 H), 6.68 (d, *J* = 16.0 Hz, 1 H), 7.25–7.50 (m, 10 H). ¹³C NMR: δ = 15.72, 64.33, 82.86, 126.93 (2 C), 127.17 (2 C), 127.94, 128.00, 128.84 (4 C), 131.00, 131.45, 136.97, 141.86. MS (EI, 70 eV): *m/z* (%) = 238 (70) [M⁺], 105 (100).

(18) **Typical Procedure for *o*-Benzenedisulfonimide-Catalyzed Esterification (Entry 5, Table 1)**

To a solution of phenylacetic acid (**5**; 0.27 g, 2.0 mmol) and butan-1-ol (0.16 g, 2.2 mmol) in toluene (10 mL) was added *o*-benzenedisulfonimide (**1**; 25 mol%; 0.11 g, 0.5 mmol) and the reaction mixture was stirred at 90 °C for 30 min. After the usual workup, the crude residue was chromatographed on a short column (PE–Et₂O, 8:2) to provide pure butyl phenylacetate (**6a**; GC, GC-MS, TLC, ¹H NMR) in 90% yield (0.38 g); colorless oil with spectral data identical to those reported.^{22d} ¹H NMR: δ = 0.85 (t, *J* = 7.0 Hz, 3 H), 1.23–1.34 (m, 2 H), 1.48–1.58 (m, 2 H), 3.56 (s, 2 H), 4.04 (t, *J* = 6.6 Hz, 2 H), 7.15–7.28 (m, 5 H). ¹³C NMR: δ = 13.86, 19.27, 30.80, 41.66, 64.94, 127.21, 128.72 (2 C), 129.43 (2 C), 134.40, 171.88; MS (EI, 70 eV): *m/z* (%) = 192 (5) [M⁺], 91 (100).

(19) (a) **Typical Procedure for *o*-Benzenedisulfonimide-Catalyzed Acetalization (Entry 10, Table 1)**

To a solution of 4-chlorobenzaldehyde (**7a**; 0.28 g, 2 mmol) and ethane-1,2-diol (**9**; 0.37 g, 6 mmol) in toluene (5 mL) was added *o*-benzenedisulfonimide (**1**; 1 mol%; 0.0044 g,

0.02 mmol) and the reaction mixture was stirred at 90 °C for 60 min. The reaction mixture was treated with solid NaHCO₃, evaporated under reduced pressure, and the residue was poured into Et₂O–H₂O (40 mL, 1:1). The aqueous layer was separated. The organic extract was dried over Na₂SO₄, and evaporated under reduced pressure; the crude residue was chromatographed on a short column (PE–Et₂O, 9.5:0.5) to provide pure 4-chlorobenzaldehyde ethylene acetal in 87% yield (**8d**; 0.32 g); colorless oil with spectral data identical to those reported.^{19b} ¹H NMR: δ = 3.92–3.99 (m, 2 H), 4.02–4.09 (m, 2 H), 5.72 (s, 1 H), 7.29 (d, *J* = 8.8 Hz, 2 H), 7.36 (d, *J* = 8.6 Hz, 2 H). ¹³C NMR: δ = 65.51 (2 C), 103.21, 128.10 (2 C), 128.75 (2 C), 135.20, 136.69. MS (EI, 70 eV): *m/z* (%) = 184 (35) [M⁺], 183 (100). (b) Katritzky, A. R.; Odens, H. H.; Voronkov, M. V. *J. Org. Chem.* **2000**, *65*, 1886.

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