

Silica Sulfuric Acid/ NaNO_2 as a Novel Heterogeneous System for the Nitration of Phenols under Mild Conditions

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Abstract: Nitrophenols can be obtained in moderate to high yields via nitrosation-oxidation of phenols with silica sulfuric acid, NaNO_2 and wet SiO_2 at room temperature. *In situ* generation of HNO_2 and a radical cation mechanism via the nitrous acid catalyzed (NAC) pathway appear to be applicable to phenol nitration using these reagents.

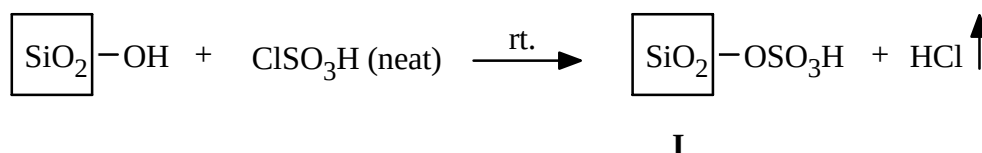
Keywords: Silica sulfuric acid, nitrosation-oxidation, nitration, nitrophenols.

Introduction

In several industrially important processes (*e.g.* nitration, nitrosation, etc.) a large excess of sulfuric acid is required because the water by-product slows the reaction down by diluting the acid. At the end of these processes, a large amount of “spent acid” is obtained which, in batch reactions, is usually neutralized and disposed of, while, in continuous processes, it has to be recycled by complex techniques. Also, the separation of the products from the acid is often a difficult and energy consuming process that habitually implies a basic aqueous work-up. Moreover, sulfuric acid is corrosive and is dangerous to transport and handle. Consequently, any reduction in the amount of sulfuric acid needed and/or any simplification in handling procedures would be highly convenient in terms of risk reduction, economic advantages and environment protection [1]. On the other hand, there is intense current research and general interest in heterogeneous systems because of the perceived opportunities

such systems present for basic research and because of the unquestioned importance such systems have in industry and in developing technologies [2]. In continuation of our studies on the application of inorganic acidic salts we found that silica gel reacts with chlorosulfonic acid to give silica sulfuric acid (**I**). It is interesting to note that the reaction is easy and clean, not requiring any work-up procedure because the evolved HCl gas can be removed from the reaction vessel immediately (Scheme 1).

Scheme 1



We believed that the silica sulfuric acid (**I**) is a superior proton source to all of the reported acidic solid supports or acidic resins such as polystyrene sulfonic acid and Nafion-H [3] for running reactions under heterogeneous conditions. Therefore, we were interested in using this inorganic acidic resin (**I**) as a new sulfuric acid function immobilized on the surface of silica gel via covalent bonding for the *in situ* generation of HNO₂ when used in conjunction with NaNO₂, wet SiO₂.

The nitration of aromatic compounds may be achieved with many nitrating reagents and is a very useful reaction in organic synthesis. Nitration of the phenol as a special case has been studied using various nitrating agents under different conditions [4-20]. Recently, in this connection we have reported the applications and mechanism of reaction of some hydrated metal nitrates and their dinitrogen tetroxide complex analogues for the nitration of phenols under various conditions [21]. We have also demonstrated that *in situ* formation of HNO₃ is a major factor for effective nitration of phenols with metal nitrates (containing covalent nitrato groups) [21a].

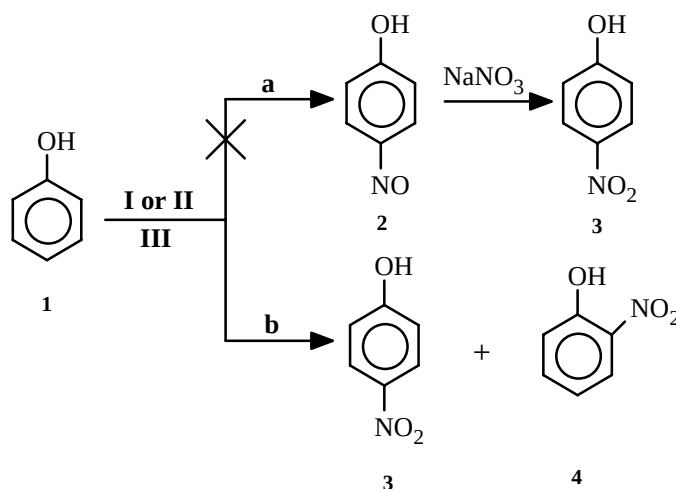
Our goal, in undertaking this line of work, was two-fold: a) to overcome the limitations and drawbacks of the reported methods such as: tedious work-up [12,14], strongly acidic media (H₀ ~ -8) [7b], oxidation ability of the reagents and safety problems (storage, handling, use and also presence of toxic transition metal cations such as Cr⁺³, Hg⁺², Cu⁺², etc., within molecular structure of the reagents) [22,23]; (b) moreover, high-yielding one-pot synthesis of nitrophenols using a novel combination of reagents are our main interest.

Very recently, we among many others, have demonstrated that heterogeneous reagent systems have many advantages such as simple experimental procedures, mild reaction conditions and minimization of chemical wastes as compared to their liquid phase counterparts. We have reported simple procedures for *in situ* generation of the nitrosonium ion (NO⁺) under mild and heterogeneous conditions and also applications of it for different purposes [24]. Therefore, we decided to seek a heterogeneous system for the nitration of phenols, and we have investigated a number of different reaction conditions based upon the *in situ* generation of HNO₂ by the relatively strong *solid inorganic acidic resin* [silica sulfuric acid (**I**)] with sodium nitrite. We wish to report here a one-pot heterogeneous procedure for the nitration of phenols.

Results and Discussion

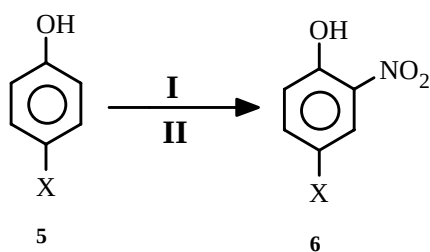
During the course of our studies on the utilization of NO^+ in functional groups transformations, we *thought* that phenol (**1**) must be converted in to the *p*-nitrosophenol selectively in CH_2Cl_2 as solvent by silica sulfuric acid (**I**) [(2 eq), one equivalent of **I** was needed for oxidation step], NaNO_2 [(**II**), (1 eq)] and wet SiO_2 (50% w/w) via *in situ* generation of HNO_2 . On the other hand, we also *thought* that phenol nitrosation is rapid and yields almost entirely the *para*- isomer which can be readily converted to *p*-nitrophenol via a mild oxidation with HNO_3 [25], $\text{H}_2\text{O}_2/\text{Na}_2\text{WO}_4$ [26], etc. Therefore, we decided to produce *p*-nitrophenol via a nitrosation-oxidation strategy [22-24] in a one pot reaction under mild and heterogeneous conditions. We chose silica sulfuric acid (**I**) because it is an excellent acid source(a proton source for the *in situ* generation of HNO_2 and NO^+ under completely heterogeneous conditions). NaNO_3 (1eq) was *needed for the second step*, i.e., *in situ* generation of HNO_3 for the oxidation of *p*-nitrosophenol. (Scheme 2, path **a**). In contrast to the reported procedures in aqueous media [26- 27], we observed that nitrosation and oxidation were occurring simultaneously. Hence, in this reaction mono nitration has occurred and *o*-nitrophenol (**4**) and *p*-nitrophenol (**3**) were obtained (Scheme 2, Table 1, path **b**).

Scheme 2



Different kinds of 4-substituted phenols (**5**) were also subjected to nitration reaction in the presence of silica sulfuric acid (**I**), NaNO_2 (**II**), and wet SiO_2 (50% w/w) in dichloromethane (Scheme 3). The nitration reactions were performed under mild and completely heterogeneous conditions at room temperature in moderate to excellent yields (Scheme 3, Table 1). The present nitration reactions can be readily carried out by placing the nitrating agents, phenols (**1** or **5**) and the solvent used in a reaction vessel and efficiently stirring the resultant heterogeneous mixture at room temperature. The mono nitrophenols can be obtained by simple filtration and then evaporation of the solvent. This method provides nitrated phenols directly, in short reaction times and good yields.

Scheme 3



5	a	b	c	d	e	f	g	h	i	j	k
X	F	Cl	Br	CN	Ph	CH ₃	OCH ₃	COCH ₃	CH ₂ Ph	NHOAc	4-HOC ₆ H ₄ -

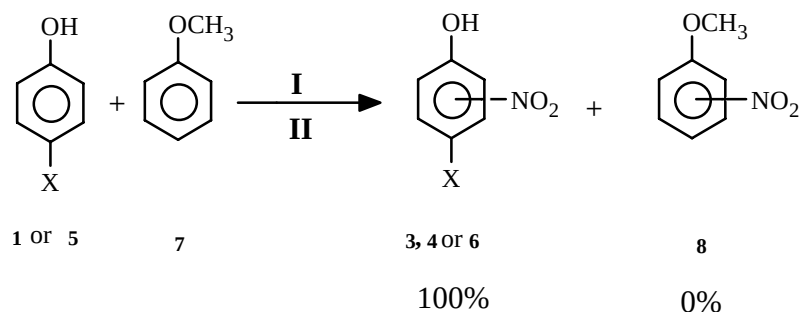
Table 1. Mononitration of Phenols to Their Corresponding Nitro derivatives with a Combination with Silica Sulfuric acid (I), NaNO₂ (II) and Wet SiO₂ (50% w/w) in Dichloromethane at Room Temperature.

Entry	Substrate	Products	Time (h)	Yields ^b %	M.p. (°C)	
					Found	Reported
1	1	3	1.5	20	110-113	115 [10]
		4		30	44-45	44 [10]
2	5a	6a	1.5	30	73	73-74 [7c]
3	5b	6b	2	45	89	91 [14, 31]
4	5c	6c	2	90	87	84 [14, 31]
5	5d	6d	2	80	140-142	145 [7c, 31]
6	5e	6e	2	86	61-63	66 [34]
7	5f	6f	2	70	29-31	31 [14, 31]
8	5g	6g	2	54	54-56	-- [31, 35]
9	5h	6h	3	62	122-124	123 [14, 31]
10	5i	6i	3	70	61-6	---[35]
11	5j	6j	24	60	180	---[16, 37]
12	5k	6k	3	25	180-184	---[34]
13	1	3, 4	24(h)	No reaction ^c	---	---

^a Wet SiO₂ : substrate (1) (0.2 g : 1mmol) . ^bIsolated Yields. ^c Reaction did not occur in the absence of Silica Sulfuric acid (I).

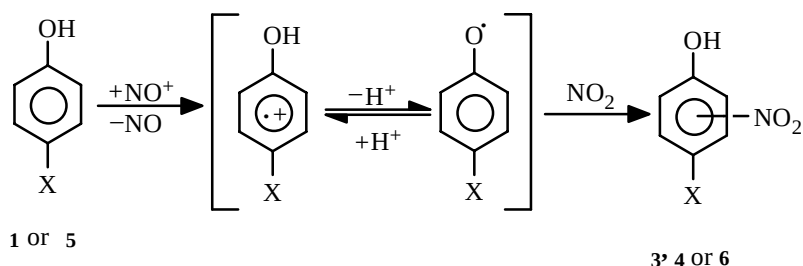
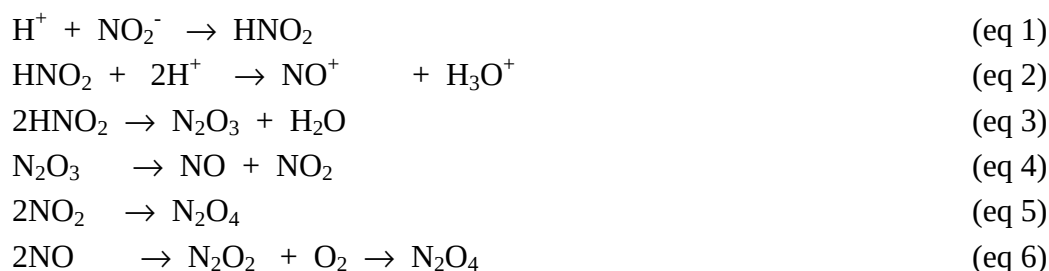
In fact, a combination of sodium nitrite and silica sulfuric acid (I) can act as *solid HNO₂* which can be readily weighed, handled and used for different purposes in the presence of moist SiO₂ [24]. A competitive reaction was performed between phenol and anisole. It was observed that exclusive phenol nitration proceeded, anisole remaining intact in the reaction mixtures after 24 hours (Scheme 4). Selective mononitration of 4,4'-dihydroxydiphenyl (5k) was also achieved by controlling the stoichiometry of reagents (Table 1, Entry 12).

Scheme 4



Although the reaction occurs without wet SiO₂, the reaction times are very long, taking several days to go to completion. Therefore, we think that the wet SiO₂ acts as an effective heterogeneous surface for *in situ* generation of HNO₂. It also makes work-up easy. This new system i.e. a combination of silica sulfuric acid (**I**) and sodium nitrite is similar to N₂O₄ (N₂O₄ ⇌ NO⁺NO₃⁻) [30] as a nitrosating agent via *in situ* generation of HNO₂ (eq 1) and NO⁺ (eq 2). Thus, on the basis of our observations, the previously reported results concerning the applications of N₂O₄ [28, 29], metal nitrate dinitrogen tetroxide complexes [M(NO₃)_m.nN₂O₄] [20a], oxidation of HNO₂ with oxygen and production of N₂O₄ (eq 3-6) [30], the very recent reported mechanism for nitration of phenols [31-33] and the products which are obtained, the following nitrous acid catalyzed mechanism (**NAC**) may be proposed (Scheme 5).

Scheme 5



Conclusions

The cheapness and the availability of the reagents, easy and clean work-ups and good yields make this method attractive for large-scale operations. Moreover, a new feature here is the fact that the reaction is heterogeneous. This could be worthwhile in an industrial setting [20].

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Experimental

General

Chemicals were purchased from the Fluka, Merck and Aldrich chemical companies. Yields refer to isolated pure products. The nitration products were characterized by comparison of their spectral (IR, ^1H -NMR, ^{13}C -NMR), TLC and physical data with the authentic samples [7, 21].

Preparation of silica sulfuric acid (I) [38]

A 500 mL suction flask equipped with a constant-pressure dropping funnel and a gas inlet tube for conducting of HCl gas over an adsorbing solution (i.e. water) was used. It was charged with silica gel (60.0 g). Chlorosulfonic acid (23.3 g, 0.2 mol) was added dropwise over a period of 30 min at room temperature. HCl gas immediately evolved from the reaction vessel (Scheme 1). After the addition was completed the mixture was shaken for 30 min. A white solid of silica sulfuric acid (76.0 g, ~100%) was obtained.

Typical procedure for the mononitration of phenol (1) with silica sulfuric acid (I), NaNO_2 (II) and wet SiO_2

A suspension of compound **1** (0.188 g, 2 mmol), **I** (1.25 g), **II** (0.138 g, 2 mmol) and wet SiO_2 (50% w/w, 0.2 g) in CH_2Cl_2 (10 mL) was stirred magnetically at room temperature. The reaction was completed after 1.5 hours and then filtered. The residue was washed with CH_2Cl_2 (2 x 10 mL). Anhydrous Na_2SO_4 (3 g) was added to the filtrate. After 15 minutes the resulting mixture was also filtered. Dichloromethane was removed by water bath (35–40 °C) and simple distillation. The residue is a mixture of 2- and 4-nitrophenols. 4-Nitrophenol (**3**) is insoluble in *n*-pentane, 0.056 g, 20% mp 112–113 °C (lit. [10] mp 114 °C). The *n*-pentane was evaporated by water bath (35–40 °C), to give 2-nitrophenol (**4**), 0.082 g, 30%, mp 43–45 °C (lit. [10] mp 44 °C) (Table 1, Scheme 2).

Typical procedure for the mononitration of 4-chlorophenol (5b) with silica sulfuric acid (I), NaNO_2 (II) and wet SiO_2 .

A suspension of compound **5b** (0.257 g, 2 mmol), **I** (1.25 g), wet SiO_2 (50% w/w, 0.2 g) and **II** (0.138 g, 2 mmol) in dichloromethane (10 mL) was stirred at room temperature for 1.5 hours (the

progress of the reaction was monitored by TLC) and then filtered. Anhydrous Na₂SO₄ (3 g) was added to the filtrate. After 15 minutes the resulting mixture was also filtered. Dichloromethane was removed by water bath (35–40 °C) and simple distillation. The yield of crystalline pale yellow solid (**6b**) was 0.156 g, (45%), mp 88 °C, (lit.[7c] mp 91 °C). ¹H-NMR (FT-90 MHz, CDCl₃, TMS) : δ 7.12 (dd, 1H), 7.42 (dd, 1H), 8.02 (s, 1H), 10.31 (b, 1H). ¹H-NMR spectra were identical with reference spectra [7c].

References

1. Riego, J.M.; Sedin, Z.; Zaldivar, J.M.; Marziano, N.C.; Tortato, C. *Tetrahedron Lett.* **1996**, *37*, 513.
2. Turro, N.J. *Tetrahedron* **1987**, *43*, 1589.
3. Olah, G.A.; Molhotra, R.; Narang, S.C. *J. Org. Chem.* **1987**, *43*, 4628.
4. Gu, S.; Jing, H.; Wu, J.; Liang, Y. *Synth. Commun.* **1997**, *27*, 2793.
5. Smith, K.; Musson, A.; DeBoos, G.A. *Chem. Commun.* **1996**, 469.
6. Waller, F.G.; Barrett, A.G.M.; Braddock, D.C.; Ramprasad, D. *Chem. Commun.* **1997**, 613, and references cited therein.
7. (a) Delaude, L.; Laszlo, P.; Smith, K. *Acc. Chem. Res.* **1993**, *26*, 607; (b) Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121. (c) Cornelis, A.; Laszlo, P.; Pennetreau, P. *Bull. Soc. Chim. Belg.* **1984**, *93*, 961.
8. Zeegers, P.J. *J. Chem. Ed.* **1993**, *70*, 1036.
9. Pervas, H.; Onysiuka, S.O.; Rees, L.; Rooney, J.R.; Suckling, G.J. *Tetrahedron*, **1988**, *44*, 4555.
10. Furniss, B.S.; Hannaford, A.J.; Smith, P.W.G.; Tatchell, A.R. “*Vogel’s Text Book of Practical Organic Chemistry*” 4th Ed; Longman: London & New York, **1986**.
11. Bruice, T.C.; Gregor, M.G.; Walters, S.L. *J. Am. Chem. Soc.* **1986**, *90*, 1612.
12. Crivello, J.V. *J. Org. Chem.* **1981**, *46*, 3056.
13. Oueartani, M.; Girad, P.; Kagan, H.B. *Tetrahedron Lett.* **1982**, *23*, 4315.
14. Poirier, J.M.; Vottero, C. *Tetrahedron*, **1989**, *45*, 1415.
15. Thompson, M.J.; Zeegers, P.J. *Tetrahedron*, **1989**, *45*, 191.
16. Tapia, R.; Torres, G.; Valderrama, J.A. *Synth. Commun.* **1986**, *16*, 681.
17. Gaude, D.; Goallar; R.L.; Pierre, J.L. *Synth. Commun.* **1986**, *16*, 63.
18. Gigante, B.; Prazeres; A.O.; Marcelo-Curto, M.J. *J. Org. Chem.* **1995**, *60*, 3445.
19. Rodrigues, J.A.R.; Filho, A.P.O.; Moran, P.J.S. *Tetrahedron*, **1999**, *55*, 6733.
20. Riego, J.M.; Sedin, Z.; Zaldivar, J.M.; Marziano, N.C.; Tortato, C. *Tetrahedron Lett.* **1996**, *37*, 513.
21. (a) Zolfigol, M.A.; Iranpoor, N.; Firouzabadi, H. *Orient. J. Chem.* **1998**, *14*, 369; (b) Firouzabadi, H.; Iranpoor, N.; Zolfigol, M.A. *Iran. J. Chem. & Chem. Eng.* **1997**, *16*, 48; (c) Firouzabadi, H.; Iranpoor, N.; Zolfigol, M.A. *Synth. Commun.* **1997**, *27*, 3301; (d) Iranpoor, N.; Firouzabadi, H.; Zolfigol, M.A. *ibid.*, **1998**, *28*, 2773.
22. (a) Firouzabadi, H.; Iranpoor, N.; Zolfigol, M.A. *Synth. Commun.* **1998**, *28*, 377; (b) Firouzabadi, H.; Iranpoor, N.; Zolfigol, M.A. *ibid.* **1998**, *28*, 1179; (c) Iranpoor, N.; Firouzabadi, H.; Zolfigol, M.A. *ibid.* **1998**, *28*, 367; (d) Firouzabadi, H.; Iranpoor, N.; Zolfigol, M.A. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2169; (e) Iranpoor, N.; Firouzabadi, H.; Zolfigol, M.A. *ibid.* **1998**, *71*, 905.

23. (a) Laszlo, P.; Cornelis, A. *Aldrichimica Acta*, **1988**, 21, 97; (b) Cornelis, A.; Laszlo, P. *Synthesis*, **1985**, 909. (c) Laszlo, P.; Cornelis, A. *Synlett*, **1994**, 155.
24. (a) Zolfigol, M.A.; *Synth. Commun.*, **1999**, 29, 905; (b) Zolfigol, M.A.; Nematollahi, D.; Mallakpour, S.E. *ibid.* **1999**, 29, 2277; (c) Zolfigol, M.A.; Mallakpour, S.E. *ibid.* **1999**, 29, 4061; (d) Zolfigol, M.A.; Kiany-Borazjani, M.; Sadeghi, M.M.; Mohammadpoor-Baltork, I.; Memarian, H.R. *ibid.* **2000**, 30, 551; (e) Zolfigol, M.A. *ibid.* **2000**, 30, 1593; (f) Zolfigol, M.A.; Ghaemi, E.; Madrakian, E. *ibid.* **2000**, 30, 1689.
25. (a) Maleski, R.J. *Synth. Commun.* **1993**, 23, 343; (b) Maleski, R.J.; *ibid.* **1995**, 25, 2327; (c) Ross, D.S.; Hum, G.P.; Blucher, W.G. *J. Chem. Soc. Chem. Comm.* **1980**, 532; (d) Al-Obaidi, V.; Moodie, R.B. *J. Chem. Soc. Perkin Trans. 2*, **1985**, 467.
23. Suboch, G.A.; Belyaev, E.Y. *Russ. J. Org. Chem.* **1998**, 34, 288.
27. (a) Ishikawa, T.; Watanabe, T.; Tanigawa, H.; Saito, T.; Kotake, K.I.; Ohashi, Y.; Ishii, H. *J. Org. Chem.* **1996**, 61, 2774; (b) Beake, B.D.; Moodie R.B. *J. Chem. Soc. Perkin Trans. 2*, **1998**, 1, and references cited therein.
28. (a) Zolfigol, M.A.; Zebarjadian, M.H.; Chehardoli, G.; Mallakpour, S.E.; Shamsipur, M. *Tetrahedron*, **2001**, 57, 1627; (b) Zolfigol, M.A.; Zebarjadian, M.H.; Chehardoli, G.A.; Keypour, H.; Salehzadeh, S.; Shamsipur, M.; *J. Org. Chem.*, **2001**, 66, 3619; (c) Zolfigol, M.A.; Zebarjadian, M.H.; Sadeghi, M.M.; Memarian, H. R.; Mohammadpoor-Baltork, I.; Shamsipur, M. *Synth. Commun.* **2001**, 30, 929.
29. (a) Mallakpour, S.E.; Zolfigol, M.A. *Indian J. Chem.* **1995**, 34B, 183; (b) Mallakpour, S.E.; Zolfigol, M.A. *J. Sci. I. R. Iran*, **1993**, 4, 199.
30. Dorfman, Y.A.; Aleshkova, M.M. *Russ. J. Org. Chem.* **1998**, 34, 217.
31. Nonoyama, N.; Chiba, K.; Hisatome, K.; Suzuki, H.; Shintani, F. *Tetrahedron Lett.* **1999**, 40, 6923.
32. Lehnig, M. *Tetrahedron Lett.* **1999**, 40, 2299.
33. Coombes, R.G.; Diggele, A.W. *Tetrahedron Lett.* **1994**, 34, 6373.
34. Raiford, L.C.; Colbert, J.C. *J. Am. Chem. Soc.* **1925**, 47, 1454.
35. Guay, V.; Brassard, P. *J. Heterocyclic Chem.* **1987**, 24, 1649.
36. Anderson, R.A.; Dalgleish, D.T.; Nonhebel, D.C.; Pauson, P.L. *J. Chem. Res.* **1977**, 12.
37. Hancock, C.K.; Clagve, A.D.; *J. Am. Chem. Soc.* **1964**, 86, 4942.
38. Zolfigol, M.A. *Tetrahedron*, **2001**, 57, 9509.

Sample Availability: Samples of compounds **3**, **4**, **6a**, **6b**, **6d**, **6h**, **6k**, 3-nitro-4-hydroxybenzoic acid and 3-nitro-4-hydroxybenzaldehyde are available from MDPI.