

Trichloroisocyanuric Acid/ NaNO_2 /wet SiO_2 as an Efficient System for the Selective Dinitration of Phenols under Solvent-free Conditions

Mohammad Ali Zolfigol,* Elaheh Madrakian, Ezat Ghaemi

Chemistry Department, College of Science, Bu-Ali Sina University, Hamadan 65174, Post Box No 4135, Iran
Fax +98(811)8272404; E-mail: Zolfi@basu.ac.ir

Received 23 July 2003

Abstract: Dinitrophenols can be obtained via direct nitration of phenols with trichloroisocyanuric acid, NaNO_2 and wet SiO_2 at room temperature under solvent-free conditions with moderate to high yields.

Key words: trichloroisocyanuric acid, dinitrophenols, solvent-free

Nitration of aromatic substrates is a widely studied reaction of great industrial significance as many nitro-aromatics are extensively utilised and act as chemical feedstocks for a wide range of useful materials such as dyes, pharmaceuticals, perfumes, and plastics.¹ Therefore, the nitration of aromatic rings has received considerable attention of late, due to unsolved problems pertaining to regioselectivity, overnitration and competitive oxidation of substrates.² Nitration of phenol taken as a special case has been studied by various nitrating agents under different conditions.³ Very recently, two excellent procedures have been reported for the nitration of phenols, one of them using silica-polyethyleneglycols/ N_2O_4 complexes for their regioselective nitration,⁴ whereas the second one reported an ultrasonic method for the nitration of phenols.⁵

Recently, we have reported the applications of trichloroisocyanuric acid/ NaNO_2 /wet SiO_2 system for the selective mononitration of phenols under mild and heterogeneous conditions.³ Our goal, in undertaking this line of work, was three-fold: a) to overcome the limitations and drawbacks of the reported methods such as tedious work-up,^{6,7} strongly acidic media,⁸ oxidation ability of the reagents and safety problems (storage, handling, using and also presence of toxic transition metal cations such as Cr^{3+} , Hg^{2+} , Cu^{2+} , within molecular structure of the reagents),⁹ (b) to perform solvent-free organic synthesis which seems to be a highly useful technique, especially for industry possessing many advantages like: reduced pollution, low costs, as well as simplicity in process and handling (these factors are especially important in industry),¹⁰ (c) moreover, to develop an high-yielding one-pot synthesis of dinitrophenols using a novel combination of reagents.

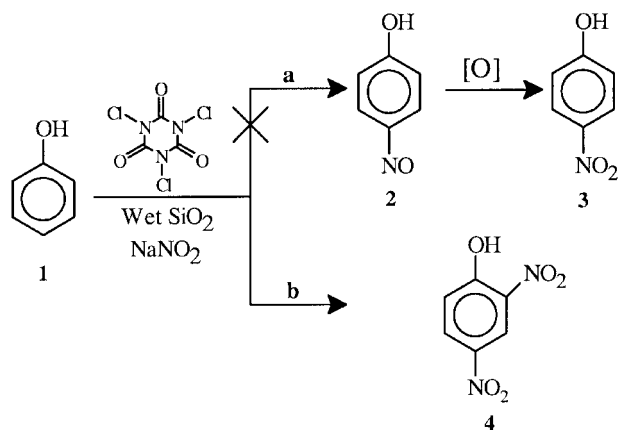
In addition, any reduction in the amount of liquid acids needed and/or any simplification in handling procedures would be highly convenient in terms of risk control, eco-

nomic advantage and environment protection.¹⁰ In continuation of our studies in this regard,¹¹ we have found that trichloroisocyanuric acid,¹² a cheap commercially available reagent used primarily as a disinfectant and deodorant, has found little application in organic chemistry so far.¹³ Therefore, we were interested in using this reagent for the dinitration of phenols when used in conjunction with NaNO_2 and wet SiO_2 under solvent free conditions, as shown in Scheme 1 and Scheme 2.

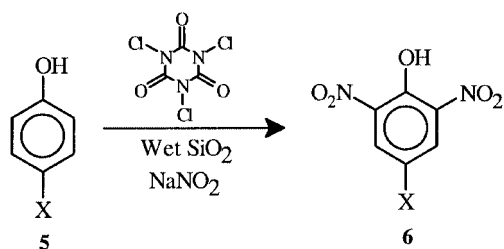
During the course of our studies concerning the utilization of NO^+ in functional groups transformations,¹¹ we thought that phenol (**1**) could be converted into the corresponding 4-nitrosoderivative **2** selectively by trichloroisocyanuric acid (**I**), NaNO_2 (**II**), and wet SiO_2 (50% w/w) under solid phase reaction via in situ generation of HNO_2 . In addition, phenol nitrosation is known to be rapid and yields almost entirely the *para* isomer which in turn can be readily converted to 4-nitrophenol (the desired product which is precursor of acetaminophene) via a mild oxidation with: HNO_3 ,¹⁴ $\text{H}_2\text{O}_2/\text{Na}_2\text{WO}_4$ ¹⁵ etc. (Scheme 1, path **a**). Therefore, we decided to produce 4-nitrophenol via a nitrosation-oxidation strategy¹⁴⁻¹⁶ in a one pot reaction under mild and heterogeneous conditions. We chose trichloroisocyanuric acid (**I**)/ NaNO_2 /wet SiO_2 system for the nitrosation of phenol (Scheme 1, path **a**) but, in contrast to the reported procedures in aqueous media,¹⁴⁻¹⁶ we observed that apparently direct formation of 2,4-dinitrophenol (**3**) occurred (Scheme 1, path **b**, Table 1). For this new system the nitrous acid catalyzed mechanism (NAC) may be proposed (see ref.¹⁷).

Different kinds of 4-substituted phenols **5** were also subjected to nitration in the presence of trichloroisocyanuric acid (**I**), NaNO_2 (**II**), and wet SiO_2 (50% w/w) under solvent free conditions (Scheme 2). The dinitration reactions were performed under mild conditions at room temperature with moderate to good yields (Scheme 1 and Scheme 2, Table 1) by simply placing the nitrating agents and phenols **1** or **5** in a reaction vessel and efficiently shaking the resulting mixture. Highly pure dinitrophenols can be obtained by simple extraction and subsequent evaporation of the solvent.

Therefore, a combination of sodium nitrite and trichloroisocyanuric acid (**I**) can act as solid nitrating agent which can be readily weighed, handled and used for different purposes in the presence of moist SiO_2 .¹¹



Scheme 1



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

Scheme 2

In conclusion, cheapness and availability of reagents, easy and clean work-up and good yields make this method attractive for organic chemists.

Chemicals were purchased from 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), TLC and physical data with authentic samples.

Dinitration of 4-Chlorophenol (5b) with Trichloroisocyanuric Acid (I), NaNO₂ (II) and Wet SiO₂: A Typical Procedure.

A mixture of compound **5b** (0.257 g, 2 mmol), **I** (0.464 g, 2 mmol), wet SiO₂ (50% w/w, 2 g) and **II** (0.276 g, 4 mmol) was shaken at r.t. for 15 min (the progress of the reaction was monitored by TLC), followed by CH₂Cl₂ (20 mL) addition and filtration of the resulting mixture. Anhyd Na₂SO₄ (3 g) was added to the filtrate and after 15 min the so obtained mixture was also filtered. CH₂Cl₂ was finally

Table 1 Dinitration of Phenols with a Combination of Trichloroisocyanuric Acid (**I**), NaNO₂ (**II**) and wet SiO₂ (50% w/w)^a under Solvent-free Conditions at Room Temperature^b

Entry	Substrate	Product	Yield (%) ^c
1	1	4	98
2	5a	6a	99
3	5b	6b	95
4	5c	6c	90
5	5d	6d	95
6	5e	6e	80
7	5f	6f	85
8	5g	6g	88
9	5h	6h	90
10	5i	6i	94
11	5j	6j	85
12	5k	6k	33
13	5l	6l	77 ^d
14	5m	6m	90

^a Substrate/reagent ratio: wet SiO₂:substrate (**1** and **5**):**I**:**II** (1 g:1 mmol:1 mmol:2 mmol).

^b All reactions were completed after 15 min.

^c Isolated yields.

^d Substrate/reagent ratio: wet SiO₂:substrate (**1** and **5**):**I**:**II** (1 g:1 mmol:1 mmol:4 mmol).

removed by water bath (35–40 °C)¹⁸ simple distillation. The residue consisted of, 0.335 g, (95% yield) of a crystalline pale yellow solid (**6b**), mp 80–81 °C, (Lit.¹⁹ mp 81 °C).

Acknowledgment

The authors gratefully acknowledge partial support to this work by the Research Affair of Bu-Ali Sina University, Hamadan, I.R. Iran.

References

- (1) Esakkidurai, T.; Pitchumani, K. *J. Mol. Catal. A: Chem.* **2002**, 185, 305.
- (2) Iranpoor, N.; Firouzabadi, H.; Heydari, R. *Synth. Commun.* **1999**, 29, 3295.
- (3) Zolfigol, M. A.; Ghaemi, E.; Madrakian, E. *Synlett* **2003**, 191; and references cited therein.
- (4) Rajagopal, R.; Srinivasan, K. V. *Ultrason. Sonochem.* **2003**, 10, 41.
- (5) Iranpoor, N.; Firouzabadi, H.; Heydari, R. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003**, 178, 1027.
- (6) Crivello, J. V. *J. Org. Chem.* **1981**, 46, 3056.
- (7) Poirier, J. M.; Vottero, C. *Tetrahedron* **1989**, 45, 1415.
- (8) Laszlo, P. *Acc. Chem. Res.* **1986**, 19, 121.
- (9) Laszlo, P.; Cornelis, A. *Synlett* **1994**, 155.
- (10) (a) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, 100, 1025.
(b) Krchnak, V.; Holladay, M. W. *Chem. Rev.* **2002**, 102, 61. (c) Varma, R. S. *Green Chem.* **1999**, 1, 43.

- (11) (a) Zolfigol, M. A. *Tetrahedron* **2001**, 57, 9509; also see our references cited therein. (b) Zolfigol, M. A.; Torabi, M.; Mallakpour, S. E. *Tetrahedron* **2001**, 57, 8381. (c) Zolfigol, M. A.; Bamoniri, A. *Synlett* **2002**, 1621. (d) Zolfigol, M. A.; Shirini, F.; Ghorbani-Choghamarani, A.; Mohammadpoor-Baltork, I. *Green Chem.* **2002**, 4, 562.
- (12) (a) Zolfigol, M. A.; Ghorbani-Choghamarani, A.; Hazarkhani, H. *Synlett* **2002**, 1002. (b) Zolfigol, M. A.; Madrakian, E.; Ghaemi, E.; Mallakpour, S. E. *Synlett* **2002**, 1633.
- (13) (a) Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H. *Synlett* **2001**, 1641. (b) Xiog, Z. X.; Huang, N. P.; Zhong, P. *Synth. Commun.* **2001**, 31, 245. (c) Mendonca, G. F.; Sanseverino, A. M.; Mattos, M. C. S. D. *Synthesis* **2003**, 41. (d) Mendonca, G. F.; Sanseverino, A. M.; de Mattos, M. C. S. *Synlett* **2003**, 45.
- (14) (a) Maleski, R. J. *Synth. Commun.* **1993**, 23, 343. (b) Maleski, R. J. *Synth. Commun.* **1995**, 25, 2327. (c) Ross, D. S.; Hum, G. P.; Blucher, W. G. *J. Chem. Soc., Chem. Commun.* **1980**, 532. (d) Al-Obaidi, V.; Moodie, R. B. *J. Chem. Soc., Perkin Trans. 2* **1985**, 467.
- (15) Suboch, G. A.; Belyaev, E. Y. *Russ. J. Org. Chem.* **1998**, 34, 288.
- (16) (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.
- (17) Zolfigol, M. A.; Bagherzadeh, M.; Madrakian, E.; Ghaemi, E.; Taqian-nasab, A. *J. Chem. Res. Synop.* **2001**, 140.
- (18) Dichloromethane is the best solvent for the extraction of dinitrophenols due to its low boiling point. We know that dinitrophenols are very volatile (due to intramolecular hydrogen bonding) and should them be distilled with high boiling point solvents the yield of reactions will result decreased.
- (19) *Dictionary of Organic Compounds*, 3th Ed., Vol. 2; Eyre and Spottiswoode: London, **1965**, 620.