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Highly efficient nitration of phenolic compounds by zirconyl nitrate ☆

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Abstract—Zirconyl nitrate was found to be an excellent reagent in the nitration of phenol and substituted phenols to give nitrated phenols. This procedure works efficiently on most of the examples at room temperature yielding nitro derivatives in fair to good yields with high regioselectivity.

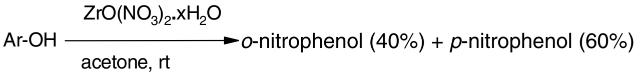
Nitration of aromatic compounds is an industrially important reaction[1] as the nitrated products are important intermediates for fine chemicals and pharmaceuticals. Nitration reactions are not usually selective and cause environmental concerns regarding the disposal of large volumes of mixed acids typically employed in this process.[2,3] A mixture of concentrated nitric acid and sulfuric acid is used as the most common nitrating reagent for the nitration of benzene, alkyl benzene, and less reactive aromatic compounds,[4] but highly reactive aromatic compounds, in particular, easily oxidized substrates such as aniline, phenols, and pyrroles, etc., require mild nitration conditions, thus a wide variety of nitrating reactions have been developed.[5] With regards to nitration of phenols, concentrated nitric acid or mixtures of acids are promising, however, their use is always associated with the formation of dinitro compounds, oxidized products, and unspecified resinous tarry materials resulting from over-oxidation of the substrate.

Further, it is noteworthy that the typical yield of direct nitration never exceeds 60%[2] because of the above-mentioned side reactions, in most cases, which makes these existing processes uneconomical.

Nitrophenols are very important organic intermediates and hence it is still interesting to develop nitrating procedures for phenolic compounds under mild conditions. Recently, various nitrating salts such as $Bi(NO_3)_3\cdot 5H_2O$,[6] $VO(NO_3)_3$,[7] $Fe(NO_3)_3\cdot 9H_2O$,[8] $(Me_4N)NO_3$,[9] $Mg(NO_3)\cdot 6H_2O$,[10] and $NaNO_3$[11] have been reported. However, except for the method reported in Ref. 6 the other procedures require either special solvents or co-reagents. In some cases, the reaction has been performed in expensive media such as ionic liquids[12] and microemulsions.[13] Therefore, it is worthwhile considering an alternative highly selective nitration process using a mild reagent such as zirconyl nitrate; it is easy to handle, cheap, and also chemically non-toxic.

In this letter, we report the direct nitration of phenol and substituted phenols using zirconyl nitrate in solution phase at room temperature (Scheme 1). The yields are good to excellent (Table 1) compared with the previous methods. The progress of the reaction was monitored by a visible change in the color of the reaction mixture and also by TLC. The results obtained substantiate a new, mild, operationally simple, and efficient method for the nitration of aromatic compounds using zirconyl nitrate as a nitrating reagent. Therefore, the present method is believed to be a good method for the synthesis of nitro compounds in organic synthesis.

Experimental procedure: To a solution of phenol (1 mmol) in acetone (5 ml) was added zirconyl nitrate



Scheme 1.

Keywords: Zirconyl nitrate; Nitration of phenols.

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Table 1. Nitration of phenols with zirconyl nitrate

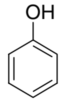
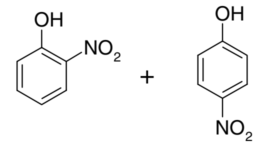
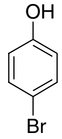
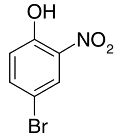
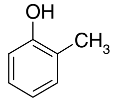
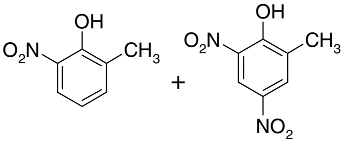
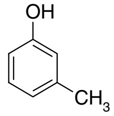
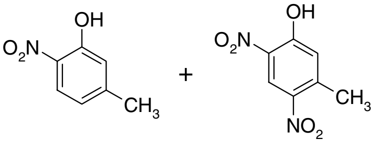
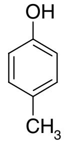
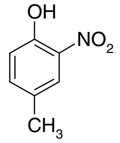
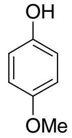
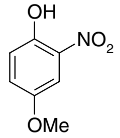
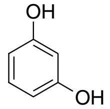
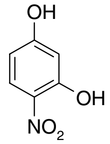
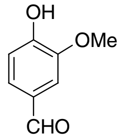
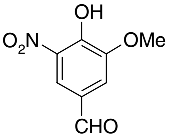
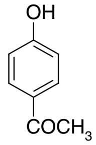
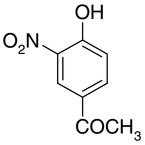
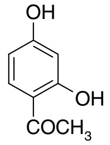
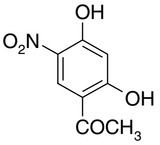
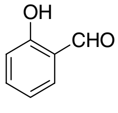
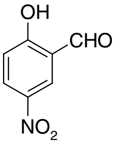
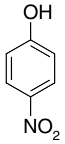
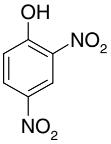
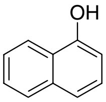
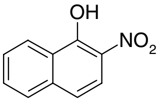
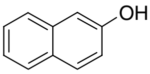
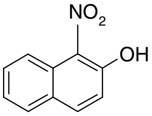
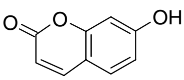
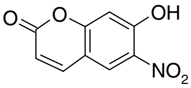
Entry	Substrate	Product[a]	Time (h) and temp. (°C)	Yield[b] (%)
1		 40% 60%	0.5, rt	100
2			0.5, rt	92
3		 43% 52%	0.45, rt	95
4		 34% 46%	1, rt	80
5			1, rt	86
6			0.5, rt	92
7			2, rt	97
8			3, rt	94
9			5, 50	84
10			5, 50	98

Table 1 (*continued*)

Entry	Substrate	Product[a]	Time (h) and temp. (°C)	Yield[b] (%)
11			2, 50	91
12			0.5, rt	88
13			3, rt	95
14			3, rt	97
15			5, 50	84

[a] All the products were characterized by ^{1}H NMR and mass spectral data.

[b] Isolated yields after silica gel chromatography.

(1 mmol) and the resulting mixture stirred at room temperature. After completion of the reaction, as monitored by TLC, the solvent was removed under reduced pressure. Water was added and the product extracted into ethyl acetate (3 × 5 ml). The combined organic layer was concentrated in vacuum to give the crude product, which was chromatographed over silica gel to give the pure compound in high yield.

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References and notes

1. Olah, G. A.; Malhotra, R.; Narang, S. C. *Nitration, Methods and Mechanism*; VCH: New York, 1989.
2. *Vogel's Text Book of Practical Organic Chemistry*, 5th ed.; Longman Group UK: Harlow, UK, 1989.
3. *Chemistry of Waste Minimization*; Clark, J. H., Ed.; Chapman and Hall: London, 1995.
4. (a) Schofield, K. *Aromatic Nitration*; Cambridge University Press: Cambridge, 1980; (b) Ridd, J. H. *Chem. Soc. Rev.* **1991**, *20*, 149–165.
5. (a) Gigante, B.; Prazeres, A. O.; Marcelo-Curto, M. J.; Cornelis, A.; Laszlo, P. *J. Org. Chem.* **1995**, *60*, 3445–3447; (b) Rodrigues, J. A. R.; de Oliveira Filho, A. P.; Moran, P. J. S.; Custodio, R. *Tetrahedron* **1999**, *55*, 6733–6738; (c) Iranpoor, N.; Firouzabadi, H.; Heydari, R. *Synth. Commun.* **1999**, *29*, 3295–3302; (d) Tasneem; Ali, M. M.; Rajanna, K. C.; Saiprakash, P. K. *Synth. Commun.* **2001**, *31*, 1123–1128; (e) Bahulayan, D.; Narayan, G.; Sreekumar, V.; Lalithambika, M. *Synth. Commun.* **2002**, *32*, 3565–3574; (f) Tanemura, K.; Suzuki, T.; Nishida, Y.; Satsumabayashi, K.; Horaguchi, T. *J. Chem. Res. (S)* **2003**, 497–499; (g) Joshi, A. V.; Baidoosi, M.; Mukhopadhyay, S.; Sasson, Y. *Org. Process. Res. Dev.* **2003**, *7*, 95–97; (h) Muathen, H. A. *Molecules* **2003**, *8*, 593–598; (i) Iranpoor, N.; Firouzabadi, H.; Heydari, R. *Synth. Commun.* **2003**, *33*, 703–710; (j) Lankaster, N. L.; Liopis-Mestre, V. *Chem. Commun.* **2003**, 2812–2813; (k) Prakash, G. K. S.; Panja, C.; Mathew, T.; Surampudi, V.; Petasis, N. A.; Olah, G. A. *Org. Lett.* **2004**, *6*, 2205–2207.
6. Sun, H.-B.; Hua, R.; Yin, Y. *J. Org. Chem.* **2005**, *70*, 9071–9073.
7. Dove, M. F.; Manz, B.; Montgomery, J.; Pattenden, G.; Wood, S. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1589–1590.
8. Rajagopal, R.; Srinivasan, K. V. *Synth. Commun.* **2003**, *33*, 961–966.
9. Shackelford, S. A.; Anderson, M. B.; Christie, L. C.; Goetzen, T.; Guzman, M. C.; Hananel, M. A.; Korneich, W. D.; Li, H.; Pathak, V. P.; Rabinovich, A. K.; Rajapakse, R. J.; Truesdale, L. K.; Tsank, S. M.; Vazir, H. N. *J. Org. Chem.* **2003**, *68*, 267–275.
10. Zolfigol, M. A.; Ghaemi, E.; Madrakian, E. *Synth. Commun.* **2000**, *30*, 1689–1694.
11. (a) Zolfigol, M. A.; Ghaemi, E.; Madrakian, E. *Molecules* **2001**, *6*, 614–620; (b) Zolfigol, M. A.; Ghaemi, E.; Madrakian, E. *Synlett* **2003**, 191–194; (c) Zolfigol, M. A.; Madrakian, E.; Ghaemi, E. *Molecules* **2002**, *7*, 734–741.
12. (a) Laali, K. K.; Gettwert, V. J. *J. Org. Chem.* **2001**, *66*, 35; (b) Handy, S. T.; Egrie, C. *Abstr. Papers Am. Chem. Soc.* **2001**, *221*, 166-IEC, part 1.
13. (a) Chhatre, A. S.; Joshi, R. A.; Kulkarni, B. D. *J. Colloid Interface Sci.* **1993**, *158*, 183; (b) Currie, F.; Holmberg, K.; Westman, G. *Colloids Surf. A* **2001**, *182*, 321.