A Mild Procedure for the Preparation of *o*-Nitrophenols by Nitro Urea or Ammonium Nitrate in the Presence of Silica Sulfuric Acid (SiO_2-OSO_3H)

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A mixture of ammonium nitrate or nitro urea and silica sulfuric acid was found to be efficient and environmentally friendly nitrating media for the preparation of *orto*-nitro phenols in dichloromethane at room temperature.

Keywords nitration, phenol, nitro urea, ammonium nitrate, silica sulfuric acid

Introduction

Nitration of aromatic compounds is one of the most fundamental and useful reactions for introducing the nitrogen atom directly into aromatic rings.[1] Nitration of aromatic compounds is an industrially important reaction as the nitrated products are intermediates for fine chemicals and pharmaceuticals.[2] The nitration of phenols is a fundamental unit process of great industrial importance generating commercially valuable intermediates and there is a great need for regio-selective pollution free processes.[3] Usually, nitrations of phenols are not region-selective and are the cause of environmental concerns regarding the disposal of large excesses of concentrated nitric acid and non-environmentally friendly metallic catalysts or reagents [such as WO_3HNO_3,[4] TiO_2-$[Ti_4H_{11}(PO_4)_9]\cdot nH_2O/HNO_3$,[5] Yb-Mo-HKSF-$HNO_3$,[6] $ZnCl_2/HNO_3$,[7] TBAB/HNO_3,[8] $Bi_5O(OH)_9(NO_3)_4/SOCl_2$,[9] $(NH_4)_2SO_4\cdot NiSO_4\cdot 6H_2O/HNO_3$,[10] ([bmim][$HSO_4$])/$NaNO_3$,[11] montmorillonite KSF/HNO_3,[12] silica sulfuric acid/$NaNO_3$[13] and Hf or Zr oxychloride complex-KSF/HNO_3[14]] in these processes. Therefore, designing systems, which reduce the mentioned problems, is of great interest.

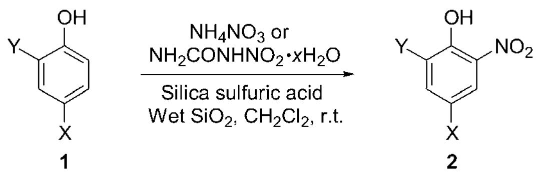
Results and discussion

Recently we have examined a variety of heterogeneous systems, generating nitroniουm ion (NO_2^+) which was used for different organic reactions.[15-21] In this light, we decided to disclose a new procedure for the nitration of substituted phenols by a mixture containing ammonium nitrate or nitro urea and silica sulfuric acid.

Ammonium nitrate is a cost, effective, nontoxic and environmentally friendly chemical, which is used in fertilizer industry and as an explosive in mining operations. Ammonium nitrate has been also applied as reagent in different chemical reactions.[22-25] Nitro urea was prepared via our newly reported procedure.[26]

Consequently, herein we decided to report a metal-free, green and heterogeneous procedure for the nitration of substituted phenolic compounds by ammonium nitrate and/or nitro urea and silica sulfuric acid under mild and heterogeneous conditions (Scheme 1).

Scheme 1



(**a**) X = Y = H; (**b**) X = Cl, Y = H; (**c**) X = F, Y = H; (**d**) X = OMe, Y = H; (**e**) X = Br, Y = H; (**f**) X = OCH_2Ph, Y = H; (**g**) X = Y = Cl; (**h**) X = CH_3, Y = Ome; (**i**) X = CH_3, Y = H; (**j**) X = Ph, Y = H; (**k**) X = $(CH_3)_3C$, Y = H; (**l**) X = $(CH_3)_2CH$, Y = H; (**m**) X = OPh, Y = H; (**n**) X = Me, Y = $(CH_3)_3C$

Result of the nitration reactions including molar ratio of reagents, time and yields of nitarated phenols are summarized in Table 1.

All of the *o*-nitrophenos were easily obtained via mixing the corresponding phenols with ammonium nitrate (NH_4NO_3) or nitro urea ($NH_2CONHNO_2$) and silica sulfuric acid (SiO_2-OSO_3H) in dichloromethane and stirring the resulting mixture at room temperature. After reaction completion, resulting yellow to orange pasty mixture was passed through the column chromatography.

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Received August 9, 2010; revised October 19, 2010; accepted December 21, 2010.

Table 1 *o*-Nitration of substituted phenols using ammonium nitrate **I** or nitro urea **II** and silica sulfuric acid **III** in dichloromethane at room temperature

Entry	Substrate	Product	Ammonium nitrate/mmol	Nitro urea/g	silica sulfuric acid/g	Time/min	Yield[a]/%
1	**1a**	**2a**	3	—	0.8	160	30
2	**1a**	**2a**	—	0.48	0.4	190	47
3	**1b**	**2b**	2	—	0.4	75	72
4	**1b**	**2b**	—	0.48	0.5	120	76
5	**1c**	**2c**	2	—	0.2	75	86
6	**1c**	**2c**	—	0.48	0.5	140	96
7	**1d**	**2d**	2	—	0.3	35	69
8	**1d**	**2d**	—	0.48	0.4	180	71
9	**1e**	**2e**	2	—	0.4	55	88
10	**1e**	**2e**	—	0.48	0.5	75	50
11	**1f**	**2f**	2	—	0.2	25	75
12	**1f**	**2f**	—	0.48	0.4	70	55
13	**1g**	**2g**	2	—	0.2	115	69
14	**1g**	**2g**	—	0.48	0.4	195	58
15	**1h**	**2h**	2	—	0.2	20	47
16	**1h**	**2h**	—	0.48	0.4	15	50
17	**1i**	**2i**	2	—	0.4	80	50
18	**1i**	**2i**	—	0.48	0.4	120	52
19	**1j**	**2j**	2	—	0.4	55	43
20	**1j**	**2j**	—	0.48	0.4	110	63
21	**1k**	**2k**	2	—	0.2	15	51
22	**1k**	**2k**	—	0.48	0.4	10	70
23	**1l**	**2l**	2	—	0.2	10	63
24	**1l**	**2l**	—	0.48	0.4	230	77
25	**1m**	**2m**	2	—	0.4	80	87
26	**1m**	**2m**	—	0.48	0.4	50	70
27	**1n**	**2n**	2	—	0.4	25	67
28	**1n**	**2n**	—	0.48	0.5	95	65

[a] Yields after purification by column chromatography.

This procedure in comparison with previously reported is a metal-free method with mild content. Also herein a wide variety of *ortho* nitro phenols has been prepared.

Plausible mechanism for the nitration of phenols by described system is outlined in Scheme 2.

To show the efficiency of the described system in comparison with previously reported procedures in the literature, we compared our obtained results for the nitration of 4-fluorophenol (as a typical example) with the best of the well-known data from the literature as shown in the Table 2.

Experimental

General

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. The nitration products were characterized by comparison of their spectral (IR, ^{1}H NMR, and ^{13}C NMR) and physical data with those of authentic samples.

Nitration of 4-bromophenol using nitro urea and silica sulfuric acid

A 10 mL round-bottom flask was charged with 4-bromophenol (0.173 g, 1 mmol), silica sulfuric acid (0.5 g), nitro urea (0.48 g) and dichloromethane (5 mL). This mixture was stirred at room temperature for 75 min (the progress of the reaction was monitored by TLC). After reaction completion, crud product was passed through the column chromatography (packed by silica gel) using CH_2Cl_2 as eluent. Solvent was removed by simple distillation and pure 4-bromo-6-nitro-phenol obtained in 50% yield (0.109 g) as crystalline pale yellow solid; m.p. 79—81 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.51 (s, 1H), 8.27 (d, J=2.4 Hz, 1H), 7.69 (dd, J=6.8, 2.4 Hz, 1H), 7.10 (d, J=8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 154.1, 140.4, 134.0, 127.3, 121.7, 111.7.

Scheme 2

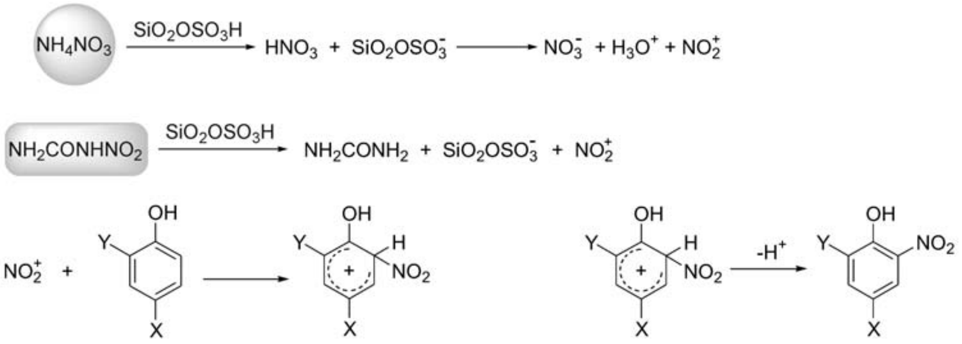

Table 2 Comparison of the different methods used for the nitration of 4-fluorophenol

Entry	Reagent and conditions	Time/min	Yield[a]/%	Reference
1	NH_4NO_3/SiO_2OSO_3H	75	86	This work
2	$NH_2CONHNO_2/SiO_2OSO_3H$	140	96	This work
3	$Mn(OAc)_2$/YbMo-HKSF	12 h	86	6
4	$[bmim][HSO_4])/NaNO_3$	30	80	11
5	Zr oxychloride complex-KSF/HNO_3	16 h	85	14
6	TBAB/ HNO_3	6 h	97	8
7	Silica chloride/$NaNO_2$	30	67	27
8	$Bi(NO_3)_3$/KSF	16	82	28

[a] Isolated yield.

Conclusion

In summary we have demonstrated that a mixture of ammonium nitrate or nitro urea and silica sulfuric acid act as mild and heterogeneous media for the *ortho*-nitration of substituted phenols. This was a convenient and environmentally friendly route to prepare substituted *ortho*-nitrophenols in high purity and reasonable yields.

Acknowledgment

Financial support for this work by the Ilam University, Ilam, Iran is gratefully acknowledged.

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(E1008098 Zhao, C.; Zheng, G.)