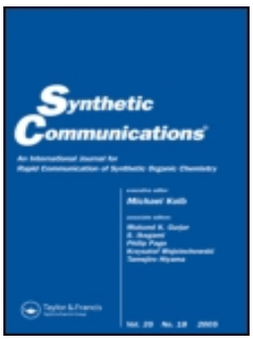

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Clay Supported Ammonium Nitrate "Clayan": A New Reagent for Selective Nitration of Arenes[#]

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ABSTRACT

The nitration of activated, deactivated and highly functionalized arenes is described using clay-supported ammonium nitrate in the presence of perchloric acid.

Key Words: Aromatic nitration; Clayan; Selective; Eco-friendly.

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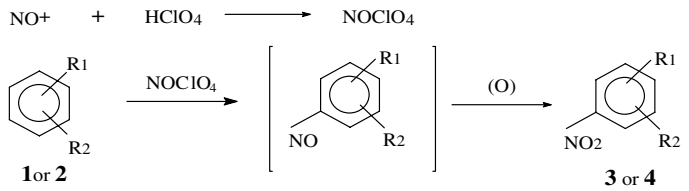

Scheme 1.

The nitration of aromatics is an important reaction in organic synthesis. It is generally performed either with nitrating mixture or by using salts of heavy metals,[1] which encounter the problem of disposal waste. In the wake of literature demand, our approach was to device a selective nitration method using inexpensive, nonmetallic reagent with minimum disposal waste. In continuation of our work on solid supported reagents,[2] herein we wish to provide a new and simple alternative for the selective nitration of arenes using "Clayan" in perchloric acid. An important purpose of this work is to refocus attention on the excellent ability of clay supported ammonium nitrate for the systematic study of nitration of activated, deactivated and highly functionalized molecules.

Nitrates in the presence of acidic clay are known to decompose into NO^+. So we presume that the NO^+ combines with $HClO_4$ to give nitrosyl perchlorate, which further reacts with arenes to give nitroso arenes. Subsequent oxidation of this leads to the nitro arene.[4]

The reaction of benzene with "Clayan" in the presence of perchloric acid, gives less yield of mono nitro benzene, but the increase of alkyl chain on benzene ring, yields are gradually increased. Further examination of highly activated systems like anisole reacts instantaneously and gave *p:o* isomers (3:1, Table 1 Entry: 8) along with demethylated nitro product (7%).[5] However, deactivated system like nitrobenzene failed to react in the same reaction condition.

We have noticed the rapid reactivity profile of anisole and unreactivity of nitrobenzene. Further examination of the substrate, having both electrons donating as well as electron withdrawing groups (Table 2 Entry: 1, 2), the reaction is indeed sluggish and proceeds at higher temperature (50°C). This may be because of the competitive effect of both activating and deactivating the functional groups.

To support the selectivity of the present method towards the highly functionalized substrates having functional groups like amides and aldehydes (Table 1: Entry 15; Table 2: Entry 3, 6) have been successfully nitrated. This protocol may find application in the synthesis of bioactive

Table 1. Selective mono nitration of substituted arenes.

Entry no.	Substituents[a]			Time (min)	Temperature (°C)	Isomeric distribution[b] (%)				Yield (%)[c]
	1[g]	R_1	R_2			2[g]	*o*	*p*	*m*	
1	**a**	H	H	30	0	**a**		mono		49
2	**b**	H	CH_3	30	0	**b**	45	55	0	70
3	**c**	H	C_2H_5	30	5	**c**	40	60	0	79
4	**d**	H	*n*-C_3H_7	45	5	**d**	20	79	0	85
5	**e**	H	*n*-C_6H_{13}	90	2	**e**	0	100	0	93
6	**f**	CH_3	*o*-CH_3	60	5	**f**	30	40	0	90[d]
7	**g**	H	OCH_3	60	−5	**g**	45	54	0	62[e]
8	**h**	H	F	60	65	**h**	25	75	0	85
9	**i**	H	CI	90	70	**i**	10	90	0	90
10	**j**	H	Br	90	70	**j**	16	84	0	92
11	**k**	H	I	90	65	**k**	45	55	0	89
12	**l**	H	CN	150	70	**l**	0	0	100	65
13	**m**	H	CH_2CN	120	67	**m**	43	54	3	79
14	**n**	H	CHO	300	70	**n**	0	0	25	25
15	**o**	*O*-OH[f]	CHO	120	35	**o**	40	60	0	85

[a]Reagent taken 1.5 equiv.
[b]Determined by G.C/^{1}H NMR.
[c]Yield of the isolated product.
[d]10% of the oxidized product is also observed.
[e]7% of the demethylated product is also observed.
[f]*o*, *p* to the hydroxyl group.
[g]Bold number given in the table are compounds numbers.

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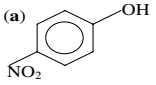
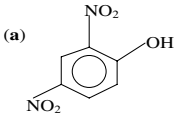
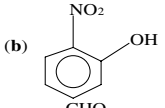
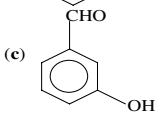
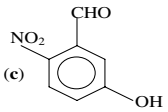
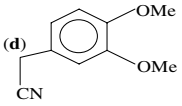
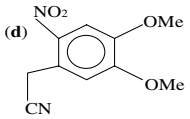
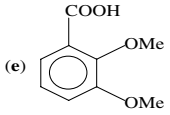
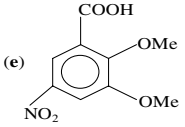
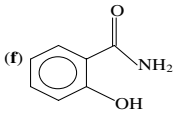
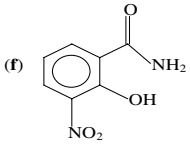
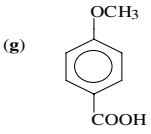
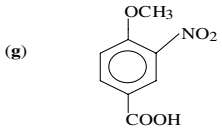
Table 2. Selective mononitration of substituted arenes.

Entry no.	3[d] Substrate	Time (min)	Temperature (°C)	4[d] Product (s)	Isolated yield (%)[a]
1		90	50		95
2		90	50	-do-	73[b]
3		100	60		69[c]
4		75	27		86
5		90	60		72
6		90	45		75
7			60		78

[a]Yield of product after the column chromatography.
[b]23% of the 2,6-dinitrophenol is observed.
[c]8% of 2-nitro-3-hydroxy benzaldehyde is observed.
[d]Bold numbers given in the table are compounds numbers.

molecules.[6] When benzamide is treated with clayan and perchloric acid at 70°C for 2 h, after workup starting material is recovered. However, the introduction of hydroxyl group (Table 2: Entry 6) ortho to the amide, leads to the nitrated product even at lower temperature.

Similarly, the nitration of benzaldehyde (Table 1: Entry 14) gives poor yield of nitro product whereas the nitration of *meta* or *ortho* hydroxy benzaldehyde proceeds smoothly with good yield. (Table 1: Entry 15; Table 2: Entry 3).

The additional feature of the procedure is strengthened, by exemplifying the nitration of haloarenes. Though various methods[1] are known for the nitration of halobenzenes, the thrust for the improvement in the *p*-selectivity has been always a demanding task.[7] The present procedure gives *p* isomer in good yield, (i.e., high *p*/*o* ratio) which is in contrast with metallic nitrate[8a] and Menke condition.[8,9] Moreover nitration of iodobenzene[9e] in very short time, shows the remarkable efficiency of present procedure (Table 1: Entry 11).

To extend the scope of the present method, we have examined the nitration of nitrile-substituted arenes. Nitration of benzonitrile gives the relatively less yield (Table 1: Entry 12) with mononitration, (G.C 97%) but extending the length of nitrile with carbon chain, (Table 1: Entry 13) the yield is boosted. Further, introduction of electron rich substituents (Table 2: Entry 4) in benzene ring enhances the yield in a highly selective fashion (G.C 92%).

In conclusion, we have demonstrated an alternative, convenient, and inexpensive method for the nitration of a variety of arenes using clay supported ammonium nitrate. The method is applicable to activated and deactivated arenes and also shows remarkable improvement in selectivity. It is worth to mention that the nonmetallic nature of the reagent and aqueous medium with minimum waste effluent shows the environmental consciousness. We have provided examples of nitration for highly functionalized arenes of biologically importance, which makes this new procedure a very attractive alternate in pharmaceutical industry. Further work is in progress to extend this procedure for other heterocyclic, and polynuclear compounds.

EXPERIMENTAL

Melting points were determined on Buchi R535 apparatus and are uncorrected. IR spectra were recorded on either Perkin-Elmer spectrophotometer or by the IR Nicole 740 FT-IR. ^{1}H NMR was recorded in Gemini 200 MHz using TMS as an internal standard. M/s recorded on Micromass 7070h or Finnigan Mat1020 B mass spectrometer operating at 70-eV. Thin layer chromatography was done on precoated silica gel 60f 254 (0.5 mm) glass plates.

Typical Experimental Procedure

Arene (1 mmol) was mixed with "Clayan"[3] (192 mg, 1.2 mmol of ammonium nitrate present in the reagent), cooled to 0°C, and perchloric acid (3 mL, 60% w/v) was added dropwise. Slurry was stirred for the stipulated time (see table) and the reaction was monitored by tlc. After completion of the reaction, reaction mixture was diluted with water, neutralized with bicarbonate solution (10%), filtered and leached with ethylacetate (2×10 mL). Organic layer was separated and dried over magnesium sulphate. Evaporation of the solvent gave the crude product, which was column purified by ethyl acetate:hexane mixture (20:80).

Spectral Data of Selected Compounds

2,4-Dinitrophenol (4a). M.p. observed 111–113°C (Literature[10a] 113°C). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 11.06 (1H, s), 9.08 (1H, d, $J = 2.68$), 8.48 (1H, dd, $J = 9.15$, 2.77, 2.52), 7.36 (1H, d, $J = 10.7$). EI-MS m/z 184 (M^+).

2-Nitro-3,5-dimethoxybenzylcyanide (4d). M.p. observed 112–114°C (Literature[8b] 111–113°C). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.98 (3H, s), 4.06 (3H, s), 4.25 (2H, s), 7.12 (1H, s), 7.75 (1H, s). EI-MS m/z 222 (M^+), 206 (M-O), 176 (M-NO_2).

2,3-Dimethoxy-5-nitrobenzoicacid (4e). M.p. observed 173–174°C (Literature[8c] 174–175°C). ^{1}H NMR (200 MHz, $CDCl_3$), δ: 8.56 (1H, d, $J = 2.45$). 7.9 (1H, d, $J = 2.69$), 4.18–4.20 (3H, s), 4.06–4.1 (3H, s). EI-MS m/z 227 (M^+).

2-Hydroxy-3-nitrobenzamide (4f).[8d] ^{1}H NMR (200 MHz, $CDCl_3$) δ: 12.25 (1H, s), 8.576 (1H, dd, $J = 5.94$, 1.96.), 8.346 (1H, dd, $J = 6.59$, 1.71), 7.267 (1H, t, $J = 8.06$, 2.28, 5.78); EI-MS m/z 182 (M^+).

4-Methoxy-3-nitro benzoic acid (4g). M.p. observed 185–187°C (Literature[8a] 186–187°C). ^{1}H NMR (200 MHz, $CDCl_3$ + DMSO-d_6), δ: 8.46 (1H, s), 8.24 (1H, dd, $J = 8.795$, 1.99, 1.95), 7.19 (1H, d, $J = 8.79$), 4.05 (3H, s). EI-MS m/z 197 (M^+).

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3. Clayan is prepared following the earlier procedure: To a solution of ammonium nitrate (5 g) in distilled water (70 mL) was added montmorillonite K10 (Aldrich Chemical Co.) 5 g in portions at room temperature and the suspension stirred for 1 h. water is removed using rotary evaporator at 50–60°C under reduced pressure and thew resulting solid was dried under vacuum at 40°C for 2 h and the reagent stored in a stoppered bottle. Detailed experimental procedure may be obtained from the Indian patent No: 56/Del/99.
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