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Guanidinium nitrate: a novel reagent for aryl nitrations

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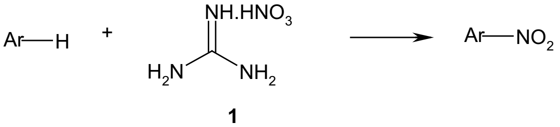
Abstract—Nitration of various aromatic compounds utilising guanidinium nitrate in 85% sulfuric acid as a nitrating agent has been studied.

Nitration reactions have acquired great importance in the chemistry of organic compounds as a number of nitro aromatics find applications as solvents, dyestuffs, pharmaceuticals, perfumery chemicals, agrochemicals, reagents and explosives. Nitro compounds also serve as useful intermediates for the preparation of other compounds, particularly amines, by reduction. Earlier work on nitration of organic compounds reports the use of nitric acid,[1] nitrosyl sulfuric acid,[2] acetyl nitrate,[3] benzoyl nitrate,[3] ethyl nitrate,[3] acetone cyanohydrin nitrate,[3] inorganic nitrates,[3] nitronium tetrafluoroborate,[3] *N*-nitropyridinium salt,[3] nitrosyl chloride,[4] nitrogen oxide,[5] urea nitrate,[6] trimethylsilyl nitrate[7] and nitrating mixtures[3] such as nitric acid–sulfuric acid, nitric acid–acetic acid, nitric acid–acetic anhydride, nitric acid–boron trifluoride and metal nitrates–acetic anhydride as the nitrating agents. It is well documented[8] that guanidinium nitrate **1** is converted into nitroguanidine by the action of sulfuric acid. Further, there is a report[9] wherein nitroguanidine was used to generate the nitronium ion in sulfuric acid. However surprisingly, **1** has never been utilised for the nitration of aromatic compounds. These observations led us to explore the potential of **1** for nitration of various aromatic compounds.

Towards this end a series of different aromatic compounds were reacted with **1** in 85% sulfuric acid at 0–5 °C to form the corresponding nitro compounds (Scheme 1, Table 1). In the first series, the reaction of **1** in 85% sulfuric acid with benzene (entry 1) and the other aromatic compounds having a weakly activating group (entry 2), activating groups (entries 3–7) and moderately deactivating groups (entries 8–10) were investigated. We found that only the mono nitrated products were obtained in good to excellent yields. Moreover in all the monosubstituted substrates (entries 3–5, 8–9) except toluene (entry 2), only the *p*-substituted nitro compounds were obtained regioselectively. Interestingly the nitration of 2-methoxyacetanilide (entry 6) and 4-methoxyacetanilide (entry 7) gave only the corresponding 5-nitro and 3-nitro substituted compounds, respectively, their 4-nitro and 2-nitro isomers were not formed. In the next series, the reaction of **1** with aromatic amines (entries 11–20) was investigated. From Table 1 it can be seen that the nitration of aniline and *m*-substituted anilines with **1** is regioselective and resulted in the formation of the corresponding *p*-nitroanilines (entries 11–13). Whereas the nitration of *o*-substituted anilines and *p*-substituted anilines with **1** gave the corresponding *m*-nitroanilines (entries 14–20) in good yields. No nitration took place at the *o*-position. Finally, the nitration of substrates having strongly deactivating group (entries 21–23) and heteroaromatic compounds such as coumarins (entries 24–26) and 2,2-dimethyl-7-hydroxy-4-chromanone (entry 27) were explored and the results obtained are shown in Table 1.



Scheme 1. Nitration of aromatic compound using guanidinium nitrate **1**.

Keywords: Guanidinium nitrate; Nitration; Regioselectivity.

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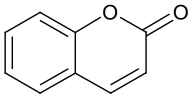
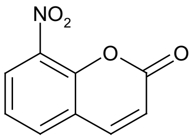
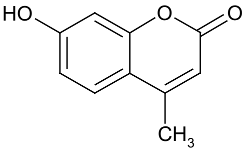
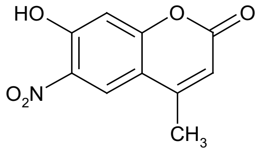
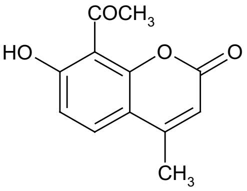
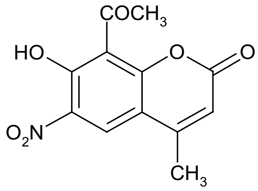
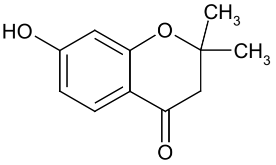
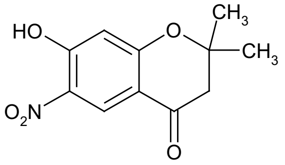
Table 1. Nitration of aromatic compounds using guanidinium nitrate **1**

Entry	Substrate	Product[a]	Time (h)	Mp[b] (°C)	Yield[c] (%)
1	Benzene	Nitrobenzene	3	—	89
2[d]	Toluene	2-Nitrotoluene	3	—	64
3	Acetanilide	4-Nitroacetanilide (3)	2.5	215	75
4	Phenol	4-Nitrophenol (4)	2	114	68
5[e]	Diphenyl ether	4,4′-Dinitrodiphenyl ether	2.5	143	55
6	2-Methoxyacetanilide	2-Methoxy-5-nitroacetanilide	2	178	81
7	4-Methoxyacetanilide	4-Methoxy-3-nitroacetanilide	2	153	82
8	Chlorobenzene	1-Chloro-4-nitrobenzene (3)	3	83	76
9	Bromobenzene	1-Bromo-4-nitrobenzene (2)	3	127	74
10	Methyl cinnamate	Methyl 4-nitrocinnamate (4)	3	161	91
11[f]	Aniline	4-Nitroaniline	0.5	148	51
12	3-Chloroaniline	3-Chloro-4-nitroaniline	1	161	72
13	3-Methylaniline	3-Methyl-4-nitroaniline	0.75	136	75
14	4-Bromoaniline	4-Bromo-3-nitroaniline	1	131	80
15	4-Chloroaniline	4-Chloro-3-nitroaniline	1	108	75
16	4-Iodoaniline	4-Iodo-3-nitroaniline	1	142	70
17	4-Methylaniline	4-Methyl-3-nitroaniline	0.75	78	72
18	4-Methoxyaniline	4-Methoxy-3-nitroaniline	0.5	57	72
19	2-Chloroaniline	2-Chloro-5-nitroaniline	1	121	76
20	2-Methoxyaniline	2-Methoxy-5-nitroaniline	0.5	118	70
21	Acetophenone	3-Nitroacetophenone	3	81	79
22	Methyl benzoate	Methyl 3-nitrobenzoate	3	78	76
23	Nitrobenzene	1,3-Dinitrobenzene	3	89	88
24			3	191	84
25[g]			3	262	41
26			3	202	85
27			3	128	39

[a] Figure in brackets indicates the percentage yield of *o*-isomer present in the crude product based on GC-analysis.

[b] Melting points are uncorrected.

[c] Yield refers to purified products.

[d] 4-Nitrotoluene (mp 57 °C) was also obtained in 18% yield.

[e] Guanidinium nitrate **1** (2 equiv) was used.

[f] 3-Nitroaniline (mp 114 °C) was also obtained in 10% yield.

[g] 7-Hydroxy-4-methyl-8-nitrocoumarin (mp 256 °C) was also obtained in 39% yield.

In conclusion a series of aromatic compounds having moderately activating, activating, weakly deactivating and strongly deactivating groups, anilines and heteroaromatic compounds have been nitrated successfully in good yields to give the corresponding nitro compounds. Experimental simplicity, mild reaction conditions, low cost of the reagent, easy handling, and absence of di-nitrated and poly-nitrated products makes **1** a useful reagent for aryl nitration.

Typical procedure: To a well-stirred mixture of aromatic compound (0.01 mol) and sulfuric acid (85%, 15 cm^3) was slowly added guanidinium nitrate **1** (1.22 g, 0.01 mol) while maintaining the temperature at 0–5 °C.

After the addition of **1** was complete, the mixture was stirred for an additional 0.5–3 h (Table 1) at the same temperature or at rt (for entries 21–23). The reaction mixture was poured onto ice water ($100\,cm^3$) and in the case of anilines it was poured onto ice cold NaOH solution (20%, $100\,cm^3$). The solid obtained was filtered, washed thoroughly with water and dried. Where solid was not obtained the aqueous layer was extracted with $CHCl_3$ ($4 \times 50\,cm^3$). The combined $CHCl_3$ layer was washed with 10% Na_2CO_3 ($2 \times 25\,cm^3$), water ($2 \times 25\,cm^3$) and then dried (anhyd Na_2SO_4). After evaporation of the solvent, a brown residue was obtained, which was purified by column chromatography to afford the corresponding nitro compound. All the compounds synthesised (entries 1–26) gave satisfactory physical and spectral data consistent with literature data.

7-Hydroxy-2,2-dimethyl-6-nitro-4-chromanone (entry 27): IR (KBr) υ: 1695, 3200 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz): δ 1.50 [s, 6H, $C(CH_3)_2$], 2.65 (s, 2H, $COCH_2$), 6.66 (s, 1H, Ar-H), 8.70 (s, 1H, Ar-H), 11.25 (s, H, OH). Anal. Calcd for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.90%. Found: C, 55.78; H, 4.52; N, 5.76%.

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