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Surface-mediated highly efficient regioselective nitration of aromatic compounds by bismuth nitrate

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Abstract

Montmorillonite impregnated with bismuth nitrate was found to be an excellent reagent for aromatic nitration in high yield. © 2000 Elsevier Science Ltd. All rights reserved.

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We have been engaged in the development of aromatic compounds as anti-tumor agents and have shown structure–activity relationships with several diamides and diamines to which a polycyclic aromatic ring was bound.[1] The nitro compounds required for the synthesis of these derivatives were prepared by the conventional nitric acid–sulfuric acid or nitroniun tetrafluoborate methods.[2] We became concerned about the disposal of the large amount of acid-waste that resulted. To avoid this complication and the associated hazards, we set out to test the nitrating abilities of nitrate-salts under solid phase conditions in a projected route to develop a simple synthesis of the nitro compound in a relatively short period of time.

Surface-mediated organic reactions are undergoing extensive investigation because they are more ecologically friendly.[3] For example, montmorillonite which is commercially available has shown considerable promise as a solid support in carrying out different chemical reactions. Montmorillonite clay impregnated with anhydrous cupric nitrate termed as ‘claycop’ was used for aromatic nitration reaction.[4] A large excess of acetic anhydride was required when claycop was used as the nitrating agent. The actual nitrating species was believed to be acetyl nitrate.[4] Similarly, a clay with ferric nitrate termed as ‘clayfen’ was used as the reagent for the nitration of estrone, though yields were poor.[5] In addition, extreme precautions were necessary for the preparation of this reagent.[6] Sulfuric acid supported on silica gel catalyzed nonselective nitration of simple aromatic compounds has also been reported.[7]

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Based on our own work on bismuth[8] salts, we became interested in exploring trivalent bismuth nitrate as the nitrating agent under solid support. These experiments have culminated in a facile synthetic method of convenient aromatic nitration by bismuth nitrate supported on montmorillonite, taking only a few minutes. We also demonstrated that bismuth nitrate-mediated nitration is effective for the nitration of polycyclic aromatic hydrocarbons.[9]

Mixing the starting materials with bismuth nitrate and montmorillonite with tetrahydrofuran and evaporation of the solvent under rotavapor comprise the reaction conditions for successful, regiospecific nitration with several aromatic compounds including multicyclic ring systems. The nitration of aromatic compounds by our method is shown in Table 1. A comparison with other solid supports, such as silica gel, acidic alumina, and ground molecular sieves was also carried out. Anisole (entry 7), naphthalene (entry 1), fluorene (entry 4), chrysene (entry 2), and dibenzofluorene (entry 3) were regiospecifically converted into the corresponding nitro compounds by bismuth nitrate–montmorillonite in excellent yield. Interestingly, the site of the electrophilic attack by this reagent was found to be identical to the conventional nitric acid or acetyl nitrate-mediated nitration reaction (Scheme 1). The reaction of naphthalene using silica gel as support under identical conditions as described with montmorillonite failed to produce the nitro derivative, although the same mixture upon microwave irradiation afforded the nitronaphthalene in 70% yield. Acidic alumina and molecular sieves alone failed to give any product with or without acid. The results indicated that montmorillonite is the solid support of choice for aromatic nitration.

$$\mathrm{ArH} \xrightarrow[\text{72-99\%}]{\text{Montmorillonite KSF-Bi(NO}_3\text{)}_3} \mathrm{ArNO_2}$$

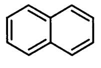
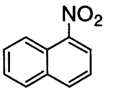
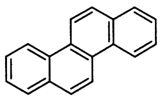
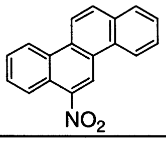
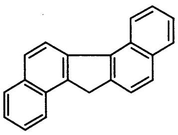
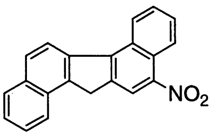
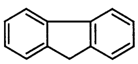
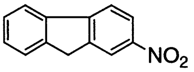
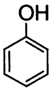
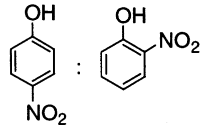
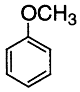
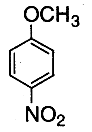
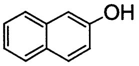
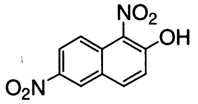
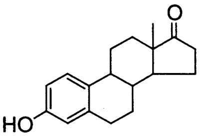
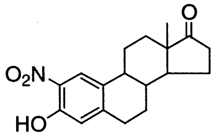
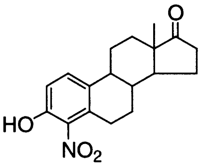
Scheme 1.

2-Naphthol (entry 7) produced only the dinitro derivative and phenol (entry 5) produced a mixture of 2- and 4-nitrophenol in a ratio of 1:3. The formation of the dinitro derivatives and mixtures of nitro derivatives with phenolic substrates indicated lesser selectivity under this condition.

In order to confirm the reactivity of phenolic substrates, we carried out nitration of estrone with bismuth nitrate–montmorillonite with the aim of synthesizing the biologically active 2 or 4-nitro estrones. In conformity with our results with phenolic substrates, the reaction produced a mixture of 2-nitro and 4-nitro estrones in a ratio of 1:1 in 94% yield (entry 8). The nitration of estrone by freshly prepared clayfen using bentonite K-10 demonstrated the production of 2-nitroestrone in 55% yield by stirring the reaction mixture in toluene overnight.[5] However, when we followed this procedure, we isolated a mixture of 2-nitro and 2,4-dinitro estrones in 90% yield (12 h).

Our results indicate that the nitration reaction depends strongly on the nature of the solid support. Further, two solid adsorbents of identical structure with different surface area (particle size) can give different product distribution. Based on a recent publication,[10] we believe that the binding of bismuth nitrate to the free hydroxyl group of the multi-metallic montmorillonite is important and that this complex produces the nitronium ion. Clearly, the failure of bismuth nitrate to produce any product with alumina and only 70% with silica gel (under microwave irradiation), despite the presence of surface hydroxyl groups, strengthens the importance of the composition of the solid support.

Table 1
Montmorillonite/Bi$(NO_3)_3$-mediated nitration of aromatic compounds

Entry	Substrate	Product	Time (min)	Yield (%)
1			10	>99
2			15	92
3			12	95
4			8	86
5		 3 : 1	10	89
6			12	91
7			15	72
8		  1 : 1	11	94

In summary, we have shown a simple, rapid and convenient method for the aromatic nitration with bismuth nitrate in the presence of montmorillonite at room temperature. The superiority of this method over others includes a very rapid reaction (approximate 30 minutes instead of 24 hour) with readily available reagents. Further, our method requires no strong acid for the preparation of the surface,[7] no acetic anhydride for the reaction[5] and it can be applied to a wide range of substrates including complex polyaromatic hydrocarbons[9] and results in high overall yield.[11]

Acknowledgements

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