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Regioselective synthesis of 4-halo *ortho*-dinitrobenzene derivatives

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Abstract

A novel method for the regioselective synthesis of 4-halo *ortho*-dinitrobenzene derivatives was developed by reacting various *meta*-halo nitrobenzenes with urea nitrate in concentrated sulfuric acid. © 2000 Elsevier Science Ltd. All rights reserved.

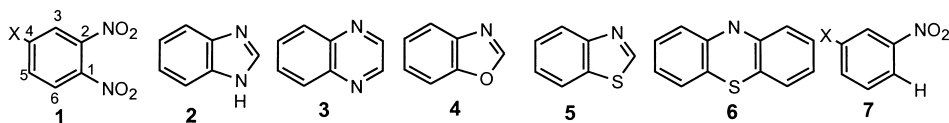
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Over the past few years we have been interested in developing methods for the synthesis of 1,2,3,4-substituted benzene derivatives which serve as useful intermediates for the synthesis of a variety of heterocyclic compounds. It is evident from the literature that appropriately substituted *ortho*-dinitrobenzenes **1** can serve as key precursors in the synthesis of heterocyclic compounds such as substituted benzimidazoles **2**, quinoxalines **3** and related compounds.¹ A halogen group of an aromatic compound can be reductively removed and also be substituted by an amine, aryl or vinyl group and also by oxygen and sulfur derived nucleophiles. It has been demonstrated that one of the nitro groups can also be displaced with some of the nitrogen, phosphorous, oxygen and sulfur based nucleophiles.² The resulting products may find use in the synthesis of heterocyclic compounds like benzoxazoles **4**, benzothiazoles **5** phenothiazines **6**. Several derivatives of **2–6** were found to possess significant biological and herbicidal activity. In order to synthesize these substituted heterocyclic compounds, we desired easy access to various substituted *ortho*-dinitrobenzenes. Traditional nitration of an aromatic nitro benzene usually produces a 1,3-dinitro derivative. This may be because of the inherent *meta*-directing nature of the nitro group.

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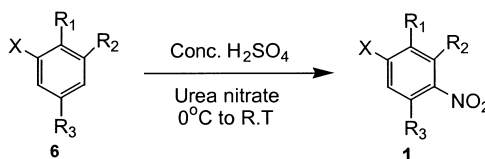
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Recently, there has been a report in which an *ortho*-nitroaniline has been converted into an *ortho*-dinitrobenzene first by converting into a sulfinimine followed by oxidation in modest yields.³



In this communication we wish to disclose a method for the regioselective synthesis of 4-halo-*ortho*-dinitrobenzene derivatives of type **1**. We have envisioned that compounds of type **1** may be obtained by selective nitration of *meta*-halo nitrobenzene derivatives of type **7**. It was reasoned that in the nitration of **7**, the halogen should direct the incoming nitro group to the *para*-position, even though it becomes *ortho* to an existing nitro group. For the sake of convenience and its proven ability to selectively nitrate anilines at the *para*-position,⁴ we decided to use urea nitrate to nitrate *meta*-halo nitrobenzenes to furnish 4-halo-*ortho*-dinitrobenzene derivatives. Our preliminary results, as shown in Table 1, confirmed that the desired *ortho*-dinitro derivatives were regioselectively produced in good yields.

Table 1



Entry	X	R ₁	R ₂	R ₃	Isolated Yield of 1
1	F	Me	NO ₂	H	94%
2	Cl	Me	NO ₂	H	93%
3	Br	Me	NO ₂	H	86%
4	F	H	NO ₂	H	77%
5	Cl	H	NO ₂	H	77%
6	Cl	CH ₂ CH ₂ OSO ₂ Me	NO ₂	H	70%
7	F	CH ₂ CH ₂ OSO ₂ Me	NO ₂	H	70%
8	Cl	Me	H	NO ₂	86%
9	Br	Me	NO ₂	H	82%

General procedure: To a solution of a *meta*-halo nitrobenzene (10 mmol) in concentrated sulfuric acid (10 ml/g) urea nitrate⁶ (1.2 to 1.5 equiv.) was introduced in small portions, maintaining the reaction temperature at around 0 to 10°C. The reaction mixture was stirred for another 10 min at the same temperature and later allowed to warm up to room temperature. Stirring continued at room temperature until the reaction went to completion (2 to 24 h) and then poured into crushed ice. The resulting products were isolated either by simple filtration or by solvent extraction.

In conclusion, a general method for the regioselective synthesis of 4-halo *ortho*-dinitrobenzene derivatives **1** from *meta*-halo nitrobenzenes has been developed. This method was found to be advantageous over some of the existing methods.^{3,5}

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