Nitrous Acid-Catalyzed Nitration of 4-Bromo-2,5-dichlorophenol. Observation of an Unusually Facile Rearrangement of a 4-Bromo-2-nitrophenol during Nitration

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Introduction

During the development of a synthesis of the non-nucleoside, HIV-1 specific reverse transcriptase inhibitor, L-697,661 (**1**)[1,2] we required easy access to the known 2-aminophenol (**2**).[2] There were several possible routes[3] to the aminophenol **2**, but we chose to examine the nitration of the readily available 4-bromo-2,5-dichlorophenol (**4**),[4] to generate the 2-nitrophenol **3**, expecting the 4-bromo substituent to undergo hydrogenolysis concomitant with reduction of the nitro group to the amine.

We report our observations on the unusual kinetic behavior of this nitration and the facile rearrangement of the product, 4-bromo-3,6-dichloro-2-nitrophenol (**3**), to the apparently thermodynamically more stable 2-bromo-3,6-dichloro-4-nitrophenol (**5**). The nitration of **4** in propionic acid with 70% HNO_3 displayed a highly variable induction period. At one extreme, an equimolar solution of **4** and HNO_3 (0.5 M) could be stirred at 30 °C for 24 h with no detectable reaction occurring. In other experiments an obvious reaction took place during addition of nitric acid to the phenol; the previously colorless solution turned yellow then orange-red accompanied by an increase in temperature of several degrees. It is well known that nitrous acid catalyzes the nitration of phenols by nitric acid.[5] Indeed, addition of a catalytic amount of $NaNO_2$ (0.2 mM) to a solution of phenol **4** (0.5 M), H_2SO_4 (0.12 M), and HNO_3 (0.05 M) in propionic acid reproducibly initiated the nitration reaction. Once initiated, the reaction was then very fast; nitric acid could essentially be titrated into the reaction mixture with excellent results (Figure 1).

After sufficient nitric acid was added to give 98−99% conversion of **4**, the product, 4-bromo-3,6-dichloro-2-nitrophenol (**3**), could be isolated in 94% yield by addition of water and filtration of the resulting crystalline solid. However, if greater than 1.0 equiv of nitric acid was added, the concentration of **3** rapidly decreased with the production of three additional compounds. The major product from the reaction in the presence of excess nitric acid was identified as 2-bromo-3,6-dichloro-4-nitrophenol (**5**). Varying amounts of **3**, 2,4-dinitro-3,6-dichlorophenol (**6**), and 2,4-dibromo-3,6-dichlorophenol (**7**) were also obtained.

Results and Discussion

Careful control of the nitration reaction conditions allowed the isolation of the desired primary product, 4-bromo-3,6-dichloro-2-nitrophenol (**3**) without formation of side products as shown in Table 1. However, a slight excess of nitric acid led to rapid formation of the isomeric phenol **5**.

Mass spectral and elemental analysis of **3** and **5** indicate these compounds are isomeric, and with the proton spectra only showing one aromatic CH and a broad phenolic resonance, ^{13}C NMR was used to distinguish these structures.[6−8]

In addition, the UV spectra were very helpful in assigning the structures of the nitrophenols. The position of the nitro group in nitrophenols can be differentiated by their UV spectrum. The 4-nitrophenols, **5** and **6**, absorb out to longer wavelengths.[9]

There are many reports of nitro groups replacing halogens during the nitration of halophenols (Zincke nitration)[10] and one reported case of the migration of a halogen from the 4 position to the 2 position during nitration,[11] although it appears to be more common in halo anisoles (Reverdin reaction).[12,13] In an attempt to understand the rapid disappearance of the desired product, we studied the rearrangement of **3** under a variety of controlled conditions (Table 3).

In addition to the nitration reagents ($NaNO_2/HNO_3$), $NaNO_2$ in propionic acid alone could initiate the rearrangement. When the reaction with $NaNO_2$ was repeated in a degassed solution of propionic acid, the rearrangement was significantly slowed, strongly suggesting the causative agent was an oxidation state of

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(3) We initially prepared **2** from 2,5-dichlorophenol via a one-pot sulfonation, nitration, desulfonation procedure, which gave the 2-nitrophenol **21**, followed by hydrogenation. Although this procedure provided **2** in a reasonable yield, the temperature required for desulfonation (>150 °C) is dangerously close to the initiation temperature of a significant exothermic decomposition of the reaction mixture. This procedure was deemed unsafe to practice on a preparative scale.

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(6) Stothers, J. B. in *Carbon-13 NMR Spectroscopy*; Academic Press: New York, 1972, p 197.

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(8) The difference in the chemical shift of a bromine bearing (−5.4 ppm) versus a nitro bearing (+19.6 ppm) aromatic carbon (relative to benzene at 128.7 ppm),[6] combined with $^1H-^{13}C$ spin−spin coupling constant data permits assignment of these isomers.[7] Although three-bond $^1H-^{13}C$ couplings constants are the largest in aromatic systems, two-bond and even four-bond couplings can be observed when electronegative substituents are on the coupling pathway. In **3**, the bromine bearing carbon at 111.6 ppm has a long-range proton splitting of 4.7 Hz, consistent with a two-bond coupling pathway. The nitro bearing carbon at 141.5 ppm, which is slightly broadened, has a long-range coupling of less than 2 Hz. Complementary data are observed in **5** where the bromine bearing carbon at 115.4 ppm is a 1.8 Hz doublet, due to a four-bond coupling pathway. The nitro bearing carbon at 140.4 ppm, is a 4.3 Hz doublet, consistent with a two-bond pathway. These data, along with the rest of the $^1H-^{13}C$ coupling constants in Table 2, permit unequivocal assignments of these structures.

(9) Pecsok, R. L.; Shields, L. D.; Cairns, T.; McWilliam, I. G. *Modern Methods of Chemical Analysis*, 2nd ed.; John Wiley & Sons: New York, **1976**; p 240.

(10) Raiford, L. C.; Miller, G. R. *J. Am. Chem. Soc.* **1933**, *55*, 2125−2131.

(11) Robertson, P. W. *Trans.* **1908**, *93*, 793.

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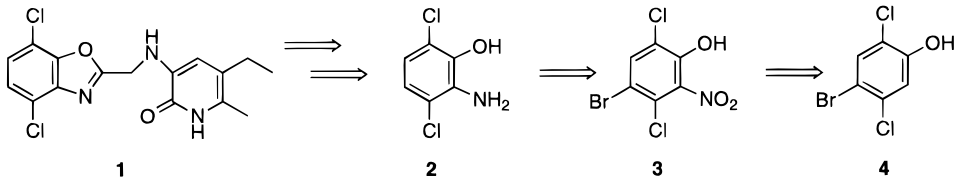
S0022-3263(96)00290-3 CCC: $12.00

Scheme 1



1 **2** **3** **4**

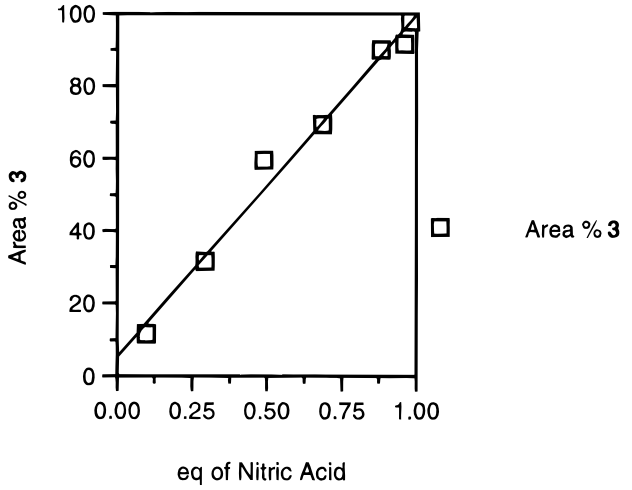
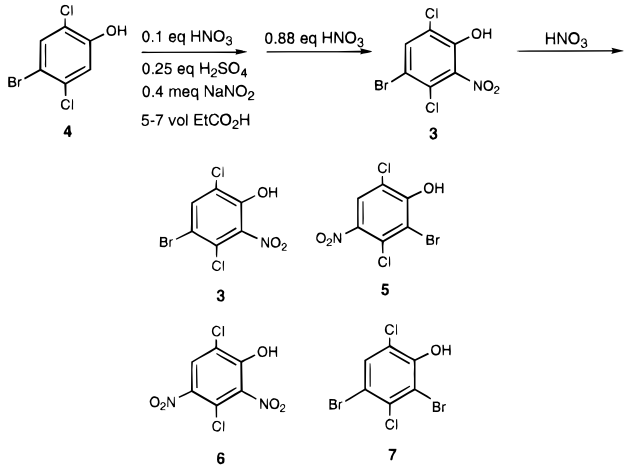


Figure 1. Equivalents of nitric acid versus area % of **3**.

Scheme 2



4 **3** **3** **5** **6** **7**

Table 1. Rearrangement of 3 In the Presence of Excess Nitric Acid

HNO_3 (equiv)	time (h)	**3** (%)	**5** (%)	**6** (%)	**7** (%)
0.98	5	94.9	<0.1	0	0
1.02	5	57.2	8.2	19.4	0
1.02	20	<0.1	56.3	22.8	<0.1

nitrogen derived from nitrite rather than nitrite itself. Milligan[14] determined that sodium nitrite in trifluoroacetic acid liberates nitric oxide. If we assume that nitric oxide is also formed in our system, then we can propose that in the presence of oxygen, nitric oxide is oxidized to nitrogen dioxide. Other oxidation states of nitrogen including nitronium and nitrosonium salts were examined and were found to have a small noncatalytic effect on **3**. Any mechanism proposed for this interesting rearrangement must account for the formation of all of the reaction products. A separate study with 2,4,5-trichlorophenol (**8**) showed that only 2-nitro-3,4,6-trichlorophenol (**9**) was produced under the reaction conditions with excess nitric acid (1.2 equiv). This demonstrates that the 4-bromo substituent or another weakly bonded substituent is required for this rearrangement to occur. The observation that 4-chlorophenols are not reactive may be attributed to the difference in the homolytic bond dissociation energy for chlorine and bromine carbon bonds (ca. 12 kcal/mol).[15]

We were interested in the relationship between the rearrangement and the mechanism of the nitration. Reaction of 4-bromo-2,5-dichlorophenol (**4**) with N_2O_4[16] in propionic acid resulted in the formation of **3** with the nitro group introduced cleanly into the ortho position. Again the same observation was made as in the nitrous acid-catalyzed nitration; as long as excess starting material remained no rearrangement was observed, but once **4** was consumed the initially formed product **3** quickly rearranged to a mixture of **3**, **5**, **6**, and **7**. Significantly, the selective ortho nitration by N_2O_4 was as equally effected in hexane solvent as in propionic acid. The exact reason for the selectivity in this radical reaction is not completely understood.

Table 2. ^{13}C Chemical Shifts and $^{1}H-^{13}C$ Spin−Spin Coupling Constants in 3 and 5[a]

	3	**5**
C_1	146.0, $^3J = 8.2$ Hz	155.7, $^3J = 8.1$ Hz
C_2	141.5, $^4J < 2$ Hz	115.4, $^4J = 1.8$ Hz
C_3	123.4, $^3J = 10.4$ Hz	126.5, $^3J = 9.0$ Hz
C_4	111.6, $^2J = 4.7$ Hz	140.4, $^2J = 4.3$ Hz
C_5	134.5, $^1J = 174.8$ Hz	126.0, $^1J = 174.8$ Hz
C_6	123.2, $^2J = 4.9$ Hz	120.0, $^2J = 5.1$ Hz

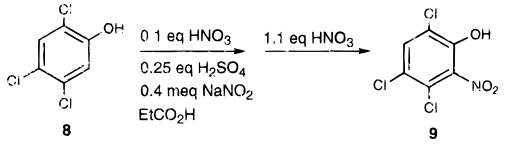
[a] Spectra run in DMSO-d_6, digital resolution for coupling constant data = 0.4 Hz/pt.

Table 3. Rearrangement of 3 with Different Additives

additive[a]	time (h)	**3** (%)	**5** (%)	**6** (%)	**7** (%)
none	0	99.3	0.2	0.3	0
$NaNO_2$[b]	1	21.6	22.8	30.7	14.9
$NaNO_2$[b]	2	1.3	50.9	28.6	7.2
$NaNO_2$[b]	3	1.3	49.4	27.1	5.2
$NaNO_2$[c]	3	65.2	5.4	6.3	15.0
NO_2BF_4[c]	3	89.6	2.7	0.2	1.4
NO_2SbF_6[c]	3	90.3	1.6	3.9	0.2
$NOBF_4$[c]	3	81.2	8.7	0	2.8
bromine[c]	0.8	36.1	42.1	3.1	4.7

[a] 0.1 equiv of additive added to a 0.5 M solution of **3** in propionic acid. [b] Atmospheric oxygen was not excluded. [c] Degassed using freeze-pump-thaw.

Scheme 3



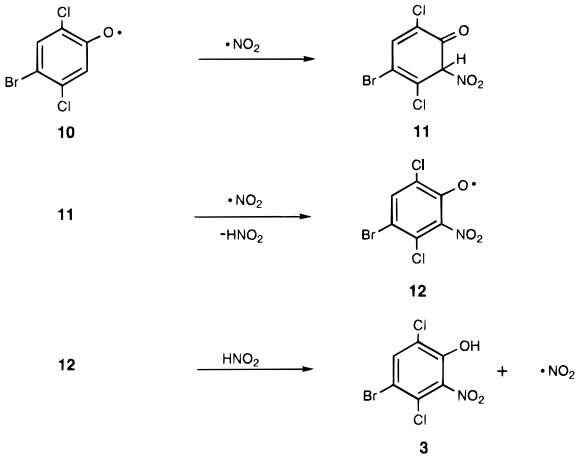
8 **9**

(14) Milligan, B. *J. Org. Chem.* **1983**, *48*, 1495−1500.

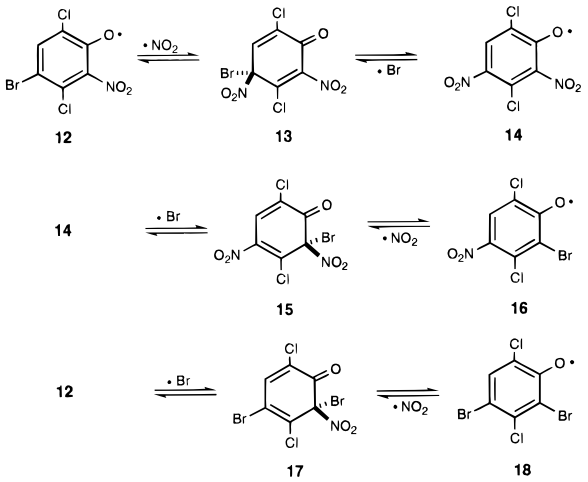
(15) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper & Row: New York, 1981; p 147.

(16) Dinitrogen tetraoxide (N_2O_4) is known to exist in equilibrium with the monomeric nitrogen dioxide (NO_2).

Scheme 4



Scheme 5



There are many similarities between nitrous acid-catalyzed nitrations and nitrations performed in the presence of nitrogen dioxide. Eberson[17] and Hartshorn[18] have both reported similar products from nitrous acid-catalyzed nitrations and nitrations involving nitrogen dioxide. We propose that the first step in the nitrous acid-catalyzed nitration is the formation of nitrogen dioxide. In this reaction nitric acid acts only as a source of nitrogen dioxide as first proposed by Titov.[19]

$$HA + NaNO_2 \rightleftharpoons NaA + HNO_2 \quad (1)$$

$$HNO_3 + HNO_2 \rightleftharpoons N_2O_4 + H_2O \quad (2)$$

$$N_2O_4 \rightleftharpoons 2 \cdot NO_2 \quad (3)$$

As nitrogen dioxide is a free radical, the next step would be the abstraction of the phenolic hydrogen to generate a phenoxy radical. There are CIDNP studies that support the formation of a phenoxy radical during nitrous acid-catalyzed nitrations of nitrophenol.[20] In addition, the 4-methyl-2,6-di-*tert*-butylphenoxy radical has been observed by EPR during the reaction of 4-methyl-2,6-di-*tert*-butylphenol with nitrogen dioxide.[21] Recently, Coombes[22] has reported a study of the mechanism of the reaction of 2,4,6-tri-*tert*-butylphenol and 2,4,6-tri-*tert*-butylphenoxy radical with nitrogen dioxide. This suggested to us that a radical reaction may in fact be operative, and we propose the mechanism as shown in Scheme 4.

Two assumptions, inherent in this mechanism, are that nitrogen dioxide addition to **10** shows both high positional selectivity and also high chemoselectivity such that no further reaction of **3** occurs in the presence of even low concentrations of **4**.

A radical chain reaction can be written for the rearrangement of **12** to the phenoxy radicals of **5**, **6**, and **7** as shown in Scheme 5. There are numerous reports, consistent with our observations, that during the nitration of halophenols *ipso* attack at an iodine or bromine can occur, but that chlorophenols are much less reactive.[5] Addition of nitrogen dioxide to the 4 position of **12** generates the cyclohexa-2,5-dienone **13**.

Table 4. Product Mixtures Obtained by Treatment of 3, 6, or 7 with Chain Reaction Initiators

compound	additive	time (h)	**3** (%)	**5** (%)	**6** (%)	**7** (%)
3	none	0	99.7	0.1	0.2	0
3	NBS	0.08	31.7	56.0	2.6	7.3
6	none	0	<0.1	<0.1	98.6	<0.1
6	NBS	24	2.1	40.3	46.5	2.3
7	none	0	<0.1	<0.1	<0.1	97.7
7	$NaNO_2$	1	6.7	13.9	<0.1	76.8

Loss of bromine atom from **13** generates **14**, the phenoxy radical of the dinitrophenol **6**. Addition of bromine radical to the 2 position of **14** generates the cyclohexa-2,4-dienone **15** that can lose nitrogen dioxide and generate the phenoxy radical **16**. Addition of the bromine radical to the 2 position of **12** and subsequent loss of nitrogen dioxide generates **18**, which is the phenoxy radical of the dibromophenol **7**.

Consideration of this mechanism yields a number of predictions: first, the rearrangement of **3** should be catalyzed by bromine atom as well as by NO_2 (see Table 3). Second, starting with either **6** or **7** and addition of either bromine atom or NO_2 should result in a similar rearrangement. Treatment of **3** with NBS in the presence of AIBN in propionic acid led to extensive rearrangement (Table 4); likewise, treatment of **6** with NBS/AIBN and **7** with $NaNO_2$ led to the product mixtures shown in Table 4.

Comparison of compound composition before and after treatment in Table 4 demonstrates that the rearrangement can be accomplished from several starting points. First, treatment of the bromonitrophenol **3** with NBS results in the formation of **5**−**7**. The dinitrophenol **6** rearranges under NBS catalysis, and the dibromophenol **7** rearranges when treated with sodium nitrite. This evidence strongly supports a chain mechanism because regardless of the starting point the same products are formed (Scheme 6).

Curiously, none of the monobromo or mononitro compounds (**4**, **20**−**22**) were formed (Scheme 7).

A mechanism for the nitration of **4** involving both nitrosonium ion and NO_2 cannot be excluded since one can argue any solution containing NO_2 also contains at least a small equilibrium concentration of nitrosonium ion. The fact that nitrosonium ion is a poor electrophile and **4** is a relatively electron poor substrate argues

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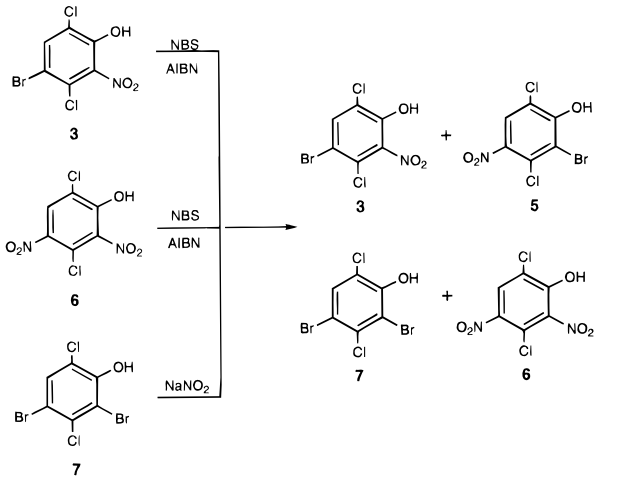
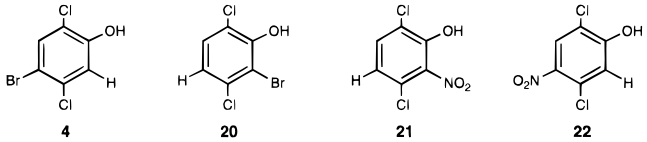
Scheme 6



Scheme 7



against a mechanism involving nitrosation. The possible role of nitrosonium ion in the rearrangement mechanism is less clear especially since nitrosonium ion alone cannot initiate this rearrangement (Table 3) and **3** is an even more electron poor substrate. Furthermore, the fact that both the nitrous acid-catalyzed nitration of **4** and the nitration of **4** with N_2O_4 have the same reaction profile suggests similar reaction manifolds.

It is significant that this rearrangement shows high positional selectivity in both propionic acid and hexane; only ortho- and para-substituted products are formed. The nitration of **4** by N_2O_4 under nonpolar conditions suggests that radical nitration may indeed be capable of high positional selectivity at least with some substrates (phenols), and that a radical nitration mechanism is worthy of more serious consideration.

Experimental Section

General. Materials were obtained from commercial sources and used without purification. HPLC analyses were performed on a Hewlett Packard Series 1050 and/or 1090 Liquid chromatograph equipped with a UV detector (210 nm), and a Zorbax RX-C8 reverse phase analytical column (4.6 cm × 250 mm). The mobile phase was acetonitrile/water, and the flow rate was 1.5 mL/min. The area percentage has been corrected for detector response, and the yields were determined with an internal standard. NMR spectra were recorded on Bruker AM-250, AM-400, and AMX-400 spectrometers. Chemical shifts are reported in ppm and for ^{1}H spectra were calibrated against the residual protium of the solvent: $CHCl_3$ (δ = 7.27) and DMSO-d_5 (δ = 2.50). Chemical shift references for ^{13}C spectra are $CDCl_3$ (δ = 77.0) and DMSO-d_6 (δ = 39.5). All coupling constants are reported in hertz (Hz). Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. Microanalysis was performed by Quantitative Technologies, Inc.

4-Bromo-2,5-dichlorophenol (**4**), 6-bromo-2,5-dichlorophenol (**10**), and 2,4-dibromo-3,6-dichlorophenol (**7**) are known compounds.[4]

2,4-Dibromo-3,6-dichlorophenol (7). A 500 mL three-neck flask equipped with an overhead mechanical stirrer, thermocouple, and a nitrogen inlet was charged with 10.0 g (61.3 mmol) of 2,5-dichlorophenol, 200 mL of methanol, and 42 μL of hydrobromic acid (48% aqueous). The solution was cooled to −20 °C, and solid *N*-bromosuccinimide (21.8 g, 122.6 mmol) was added. The temperature of the reaction mixture increased to −15 °C. The solution was cooled to −20 °C and then allowed to warm to ambient temperature over 2 h. Additional NBS was added (0.55 g, 3.1 mmol), and the reaction mixture was stirred at 23 °C for 1.75 h. The reaction mixture was concentrated *in vacuo*, and the wet yellow solids were partitioned between ethyl ether (200 mL) and water (200 mL). The separated organic layer was washed with water (200 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. A yellow solid (18.7 g) was isolated. This material (^{1}H-NMR) contained 95.6% of **7** and 4.4% of **4**. The yield corrected for purity is 90.9%. An analytical sample was prepared by recrystallizing **7** (18.1 g) from hexanes (84 mL): mp 97−98 °C (lit. mp 99−100 °C);[23] ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.63 (s, 1 H); 6.04 (s, 1 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 149.3, 134.1, 132.0, 119.4, 113.1, 112.2. Anal. Calcd for $C_6H_2Br_2Cl_2O$: C, 22.46; H, 0.63; Cl, 22.10. Found: C, 22.46; H, 0.61; Cl, 22.25.

4-Bromo-3,6-dichloro-2-nitrophenol (3). A 50 mL three-neck flask equipped with a magnetic stirrer and a thermocouple was charged with **4** (4.0 g, 16.54 mmol), propionic acid (28 mL), and sulfuric acid (228 μL, 4.13 mmol) and warmed to 30 °C. A solution of 70% nitric acid (298 μL, 5.6 M, 1.67 mmol) in propionic acid and 16 μL of an aqueous sodium nitrite solution (0.41 M, 6.6 μmol) were added, and the temperature of the reaction solution increased to 33 °C. Additional nitric acid solution (2.44 mL, 13.73 mmol) was added over a 10 min period maintaining the reaction temperature between 30−35 °C during the addition.

The reaction mixture was added dropwise to a cold (10−15 °C) saline solution (20 g sodium chloride/228 mL water) over a 10 min period. An orange solid was isolated by filtration, washed with water (3 × 5 mL), and dried *in vacuo* with a nitrogen sweep. The weight of **3** isolated was 4.46 g (94%). An analytical sample was prepared by recrystallization from cyclohexane: mp 110−112 °C; ^{1}H NMR (399.87 MHz, DMSO-d_6) δ 11.1 (v br, 1 H), 8.11 (s, 1H); ^{13}C NMR (100.56 MHz, DMSO-d_6): δ 146.0, 141.5, 134.5, 123.4, 123.1, 111.6. MS (EI, 70 eV) *m/z* 285 (M^+). Anal. Calcd for $C_6H_2BrCl_2N_2O_3$: C, 25.12; H, 0.70; N, 4.88; Cl, 24.72. Found: C, 25.19; H, 0.66; N, 4.71; Cl, 24.77.

Nitration of 4 with Nitrogen Dioxide in Propionic Acid. Nitrogen dioxide was bubbled into a solution of **4** (0.83 M) in propionic acid for 10 s. Assay by HPLC after 10 min indicated the formation of **3** (57 A%) with remaining **4** (43 A%). Continued addition of nitrogen dioxide resulted in complete conversion of **4** to **3** and eventually in the formation of dinitrophenol **6.**

Nitration of 4 with Nitrogen Dioxide in Hexanes. Nitrogen dioxide was bubbled into a saturated hexane solution of **4** (0.03 M) for 1 min. The solution was stirred at room temperature overnight and assayed by HPLC that indicated the formation of **3** (28 A%) with remaining **4** (60 A%).

2-Bromo-3,6-dichloro-4-nitrophenol (5). A 20 mL scintillation vial equipped with a magnetic stir bar was charged with 1.33 g (4.64 mmol) of **3**, 10 mL of propionic acid and 0.022 g (0.32 mmol) of sodium nitrite and capped. The hazy red-orange solution was stirred at room temperature for 2 h and then poured into saturated sodium chloride solution (10 mL). The mixture was extracted twice with ethyl ether (10 mL) and the separated ether solution was dried over anhydrous sodium sulfate. An orange solid was isolated by concentration *in vacuo* (1.27 g). This solid was recrystallized three times from cyclohexane to yield 0.86 g (65%) of **5**: mp 129−130 °C dec; ^{1}H NMR (399.87 MHz, DMSO-d_6): δ 11.34 (br s, 1 H), 8.27 (s, 1 H); ^{13}C NMR (100.56 MHz, DMSO-d_6) δ 155.7, 140.3, 126.6, 125.9, 120.0, 115.4. MS (EI, 70 eV) *m/z* : 285 (M^+). Anal. Calcd for $C_6H_2BrCl_2N_2O_3$: C, 25.12; H, 0.70; N, 4.88; Cl, 24.72. Found: C, 25.16; H, 0.65; N, 4.66; Cl, 24.52.

2,4-Dinitro-3,6-dichlorophenol (6). A 50 mL two-neck flask equipped with a condenser, nitrogen inlet, thermocouple, and a magnetic stir bar was charged with 1.63 g (10 mmol) of 2,5-dichlorophenol, 22 mL of propionic acid, 140 μL (2.5 μmol) of sulfuric acid, and 150 μL (2.4 mmol) of nitric acid. Solid sodium nitrite (20 mg, 0.29 mmol) was added to the colorless solution that quickly developed a yellow color and gas evolution was noted.

A solution of 70% nitric acid (1.5 mL, 24 mmol) in propionic acid (5 mL) was added over 5 min with a temperature increase

(23) Fox, D. L.; Turner, E. E. *J. Chem. Soc.* **1930**, 1853−1867.

from 20 °C to 35 °C. The reaction mixture was allowed to cool to 20 °C and was stirred overnight.

The reaction mixture was poured into a cold sodium chloride solution, and an orange solid was collected by filtration. The solid was washed with water and dried *in vacuo*. The product **6** was isolated in 65% yield (1.64 g). An analytical sample was prepared by recrystallization from cyclohexane: mp 142−144 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.21 (s, 1 H); ^{13}C NMR (100.56 MHz, DMSO-d_6) δ 156.9, 142.5, 130.5, 127.8, 122.6, 119.4. MS (EI, 70 eV) *m*/*z* 252 (M^+). Anal. Calcd for $C_6H_2Cl_2N_2O_5$: C, 28.48; H, 0.80; N, 11.08; Cl, 28.03. Found: C, 28.42; H, 0.85; N, 10.78; Cl, 27.86.

2-Nitro-3,4,6-trichlorophenol (9). A 50 mL two-neck flask equipped with a condenser, nitrogen inlet, thermocouple and a magnetic stir bar was charged with 4.01 g (20.3 mmol) of 2,4,5-trichlorophenol and 25 mL of propionic acid. The solution was warmed to 30 °C and 278 μL (5 mmol) of sulfuric acid, 125 μL (2 mmol) of nitric acid and 16 μL of a 0.5 M aqueous sodium nitrite solution (8 μmol) were added to the solution, which quickly developed a yellow color and exothermed to 35 °C.

Neat 70% nitric acid (1.4 mL, 22.4 mmol) was added over 1h while maintaining the temperature between 30−35 °C. The reaction mixture was allowed to cool to 20 °C, poured into a sodium chloride solution (8 g/110 mL) and an oil precipitated. The mixture was extracted with ethyl ether, washed with brine and dried over magnesium sulfate. The solvent was removed *in vacuo* to give 3.94 g of **9** (80% yield). An analytical sample was prepared by recrystallization from cyclohexane: mp 90−91 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.65 (s, 1 H), 7.56 (bs, 1 H); ^{13}C NMR (100.56 MHz, $CDCl_3$) δ 146.0, 138.1, 132.6, 125.9, 125.0, 121.7. MS (EI, 70 eV) *m*/*z* 241 (M^+). Anal. Calcd for $C_6H_2Cl_3NO_3$: C, 29.72; H, 0.83; N, 5.78; Cl, 43.87. Found: C, 29.90; H, 0.88; N, 5.54; Cl, 43.66.

Rearrangement of 3. General Procedure. One side of a J-tube reaction vessel[24] was charged with 1 mL of a 0.5 M solution of **3** (0.5 mmol) in propionic acid and the other side was charged with a magnetic stir bar and 0.054 mmol of one of the following; $NaNO_2$, NO_2BF_4, NO_2SbF_6, $NOBF_4$, or Br_2. The tubes were capped with three-way stopcocks, and the apparatus was degassed using freeze-pump-thaw techniques. The apparatus was vented to dry nitrogen, and the solution of **3** was transferred to the other side of the apparatus and mixed. Samples were removed at timed intervals for HPLC assay, and the assay results are included in Table 3.

Rearrangement of 3 with NBS/AIBN. A 1 dram screw cap vial was charged with 0.1723 g (0.6 mmol) of **3**, 0.0213 g (1.26 mmol) of NBS, 0.0001 g (0.00006 mmol) of AIBN, and 500 μL of propionic acid. This solution was stirred at room for 5 min and assayed by HPLC. The results are reported in Table 4.

Rearrangement of 6 with NBS/AIBN. A 1 dram screw cap vial was charged with 0.0265 g (0.1 mmol) of **6**, 0.0211 g (0.12 mmol) of NBS, 0.0052 g (0.03 mmol) of AIBN, and 500 μL of propionic acid. This solution was stirred at room temperature overnight and assayed by HPLC. The results are reported in Table 4.

Rearrangement of 7 with $NaNO_2$. A 1 dram screw cap vial was charged with 0.1414 g (0.44 mmol) of **7**, 0.1076 g (1.56 mmol) of sodium nitrite, and 2 mL of propionic acid. This solution was stirred at room temperature for 1 h and assayed by HPLC. The results are reported in Table 4.

Determination of the Relative Response Factors for 3, 5, 6, and 7. A 1 dram screw cap vial was charged with 0.040 mmol of **3**, 0.040 mmol of **5**, 0.041 mmol of **6**, and 0.040 mmol of **7** and dissolved in CD_3CN. Comparison of the areas from the integrated ^{1}H-NMR spectrum with the area determined by HPLC gave the relative response factors for **3**, **5**, **6**, and **7** of 1.00, 1.81, 2.32, and 1.03, respectively.

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