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Tele Nucleophilic Aromatic Substitutions in 1-Nitro-3- and 1,3-Dinitro-5-trichloromethylbenzene, and 3-Trichloromethylbenzonitrile. A New Synthesis of the 1,4-Benzothiazine-3(4*H*)-one Ring System from 3-Nitrobenzoic Acid

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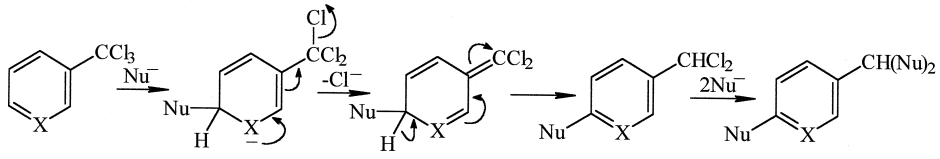
Abstract—3-Trichloromethylnitrobenzene **2**, 1,3-dinitro-5-trichloromethylbenzene **13** and 3-trichloromethylbenzonitrile **18** react with sodium methoxide to give 4-methoxy-3-nitrobenzaldehyde **6**, 4-methoxy-3,5-dinitrobenzaldehyde **15** and 5-dimethoxymethyl-2-methoxybenzonitrile **19**, respectively. Compounds **2** and **13** react with methyl thioglycolate to afford dichloromethylacetates **7** and **16**, respectively. These products are the result of *tele* nucleophilic aromatic substitution. Compound **18** reacted with methyl thioglycolate to give acetate **20** resulting from nucleophilic displacement of cyanide. Reductive cyclisation of **7** afforded benzothiazine **11**.

Nucleophilic aromatic substitution in carbocyclic and heterocyclic arenes is a very important reaction from both the academic and industrial point of view. Although the classical S_NAr reaction of aryl halides by addition-elimination has dominated the scene for over a century,[1–5] reactions following a different pathway have gained increasing interest and importance. These can be grouped into the following categories: elimination–addition (via arenes),[6] single electron transfer promoted ($S_{RN}1$) reactions,[7] photochemical reactions,[8] transition metal catalysed reactions,[9] nucleophilic ring opening and ring closure (ANRORC) reactions,[10] and more recently, *vicarious* nucleophilic substitution (VNS) of hydrogen,[11,12] *cine* nucleophilic substitution[13,14] and *tele* nucleophilic substitution.[15–18]

We have previously reported several examples of *tele* nucleophilic substitution in 3-trichloromethylpyridines.[16,17] The requisite for these reactions is a trichloromethyl group *beta* to the ring nitrogen of pyridine. Thus reaction occurs by addition of nucleophile to the 6-position, elimination of chloride ion and a 1,5-hydrogen shift from the 6-position to the exocyclic carbon leading to a 2-substituted-5-dichloromethylpyridine. The final products depend on the reaction conditions and work-up procedure, for example with alkoxides they can be acetals or aldehydes (Scheme 1).

Herein we report the reactions of 1-nitro-3-trichloromethylbenzene **2**, 1,3-dinitro-5-trichloromethylbenzene **13** and 3-trichloromethylbenzonitrile **18** with sodium methoxide and methyl thioglycolate. The products **6**, **7**, **9**, **15** and **19** are the result of *tele* nucleophilic aromatic substitution. The novel synthesis of benzothiazine **11** is also reported.



Scheme 1.

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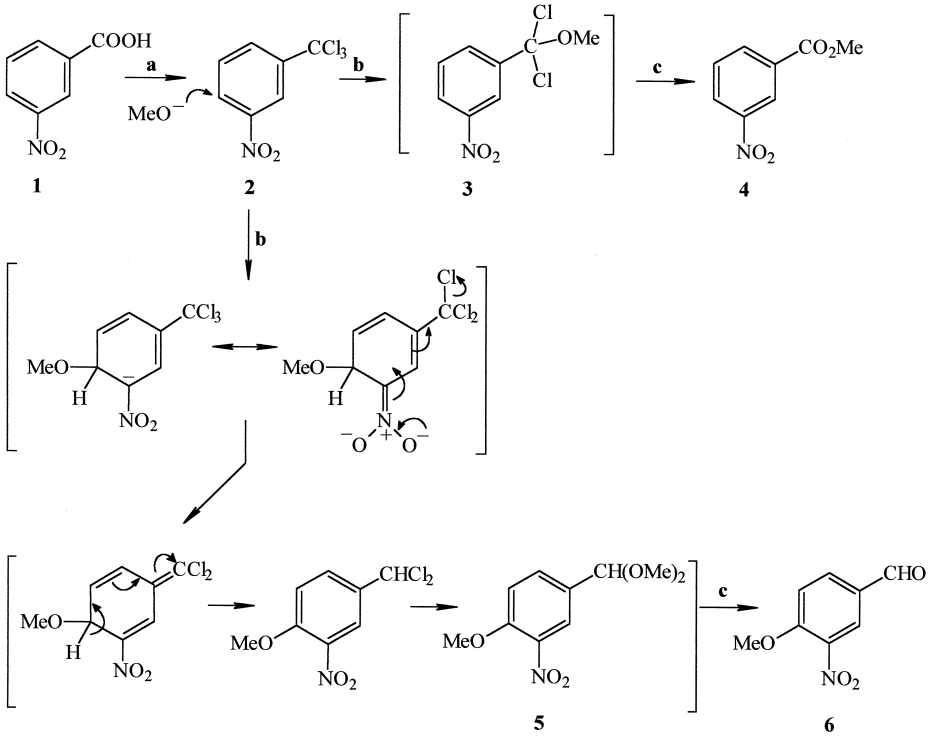
Compound **2** was prepared in no more than 50% yield by heating 3-nitrobenzoic acid **1** in a mixture of phenylphosphonic dichloride and phosphorus pentachloride. This method is described by McKendry et al.[19c] in a patent but spectroscopic and analytical data are not given. Other methods of preparing **2** are nitration of trichloromethylbenzene[19a] and Friedel–Crafts alkylation of 1-nitro-3-trifluoromethylbenzene.[19b] The reaction of **2** with one equivalent of sodium methoxide in boiling methanol gave a mixture containing ester **4** (23%) and aldehyde **6** (59%), implying that reaction occurs via the dichloromethoxymethyl compound **3** and the acetal **5**, respectively, followed by hydrolysis (Scheme 2). This is a rare case of competition between an S_N2 reaction and *tele* nucleophilic aromatic substitution. Compound **6** has previously been prepared by oxidation of (4-methoxy-3-nitrophenyl)methanol,[20] methylation of 4-hydroxy-3-nitrobenzaldehyde,[21] nitration of 4-methoxybenzaldehyde[22] and nucleophilic aromatic substitution of chloride ion from 4-chloro-3-nitrobenzaldehyde.[21a] Compound **4** is commercially available.

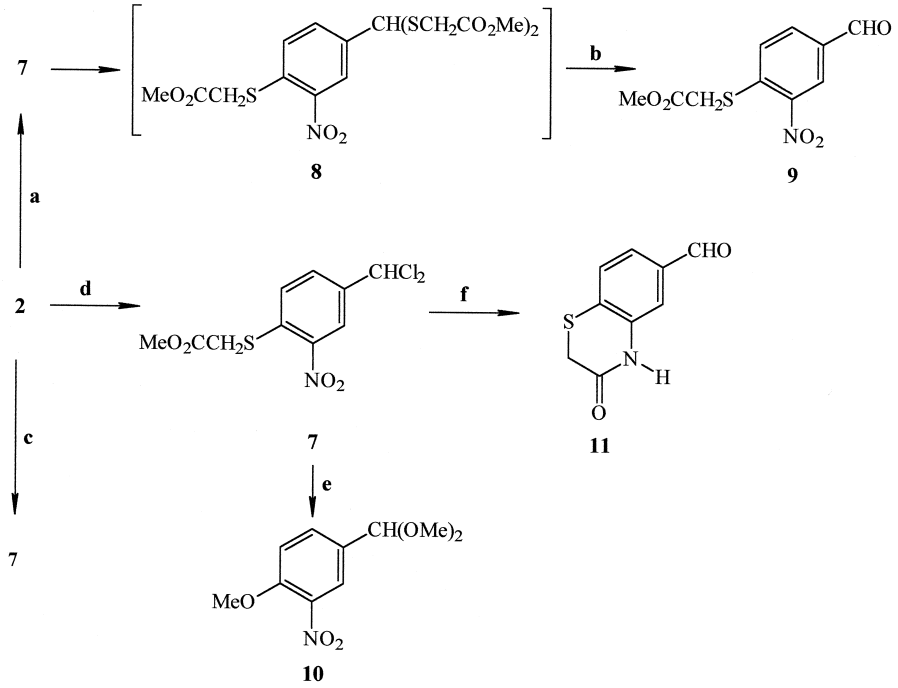
The outcome of the reaction of compound **2** with methyl thioglycolate (Scheme 3) depended on the reaction conditions. With methanol as solvent, **2** was heated under reflux with methyl thioglycolate and either triethylamine or potassium carbonate. When triethylamine was used followed by dry work-up, dichloromethyl compound **7** and starting material were isolated in 31 and 23% yield, respectively. When potassium carbonate was used followed by aqueous work-up, **7**, **9** and starting material were isolated in 12, 27 and 30% yield, respectively. The isolation of aldehyde **9** implies that reaction occurs via thioacetal **8** which was hydrolysed during work-up. On the other hand, a reaction in DMF at ambient temperature with HMPA as catalyst and triethylamine, followed by aqueous work-up, gave **7** in 67% yield, with only 18% of starting material **2**.

Nitro-ester **7** is potentially a precursor to both benzo[2,3-*b*]thiazole-*N*-oxide and 3,4-dihydro-2*H*-1,4-benzothiazin-3-one ring systems. In a first attempt to cyclise **7** to the former ring system we used triethylamine in ethanol under reflux,[23a] only to recover starting material. In a second attempt, compound **7** was heated in a methanolic solution of sodium methoxide.[23b] Instead of the hoped-for cyclisation product, acetal **10** was obtained. On the other hand, reaction of **7** with zinc and calcium chloride in aqueous methanol gave **11** in 52% yield. This three step synthesis of a 3,4-dihydro-2*H*-1,4-benzothiazin-3-one from 3-nitrobenzoic acid by sequential chlorination, *tele* nucleophilic aromatic substitution and reductive cyclisation constitutes a novel route to this ring system. Other syntheses of this ring system are reductive cyclisation of 4-acetyl-2-nitrophenylthioacetic acid with ferrous sulfate-ammonium hydroxide,[24] reaction of *o*-aminobenzenethiols with 2,4-oxetanedione,[25] treatment of zinc salts of *o*-aminobenzenethiols with chloroacetyl chloride,[26] reaction of *N*,*N*′-dialkyldithiodianilines with β-keto esters[27] and more recently by reductive cyclisation of (2-nitrophenylsulfanyl)acetic acids.[28]

The preparation and reactions of 1,3-dinitro-5-trichloromethylbenzene **13** are shown in Scheme 4. It was prepared by heating 3,5-dinitrobenzoic acid **12** with phenylphosphonic dichloride and phosphorus pentachloride. Smith et al.[29] prepared **13** by heating 1,3-dinitro-5-trifluoromethylbenzene in acetyl chloride containing anhydrous aluminium chloride. Reaction of **13** with methanolic sodium methoxide at room temperature for 24 h afforded the aldehyde **15**. Since water was excluded during the synthesis and work-up of this compound, it is proposed that acetal **14** was an



Scheme 2. Reagents: (a) $PhP(O)Cl_2$, PCl_5; (b) MeONa, MeOH, reflux; (c) H_2O.

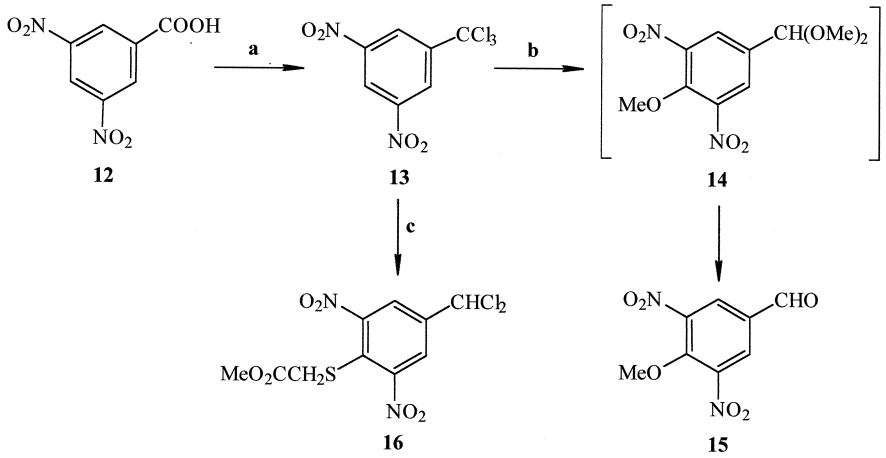


Scheme 3. Reagents: (a) $HSCH_2CO_2Me$, K_2CO_3, MeOH, reflux; (b) H_2O; (c) $HSCH_2CO_2Me$, Et_3N, MeOH, reflux; (d) $HSCH_2CO_2Me$, Et_3N, HPMA, DMF, room temperature; (e) NaOMe, MeOH, reflux; (f) Zn, $CaCl_2$, H_2O, MeOH, reflux.

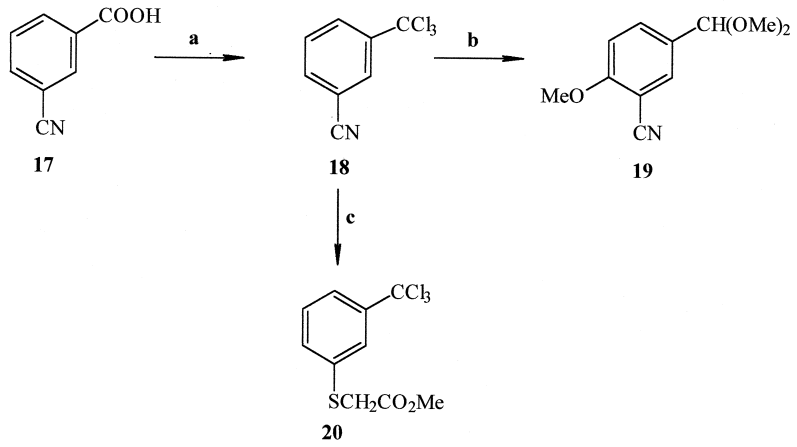
intermediate that hydrolysed during column chromatography. Similar situations were encountered in our earlier work.[17] Compound **15** has been prepared by nitrating 4-methoxybenzaldehyde,[30] by treating (4-methoxy-3,5-dinitrophenyl)methanol with formaldehyde in aqueous methanol containing sodium hydroxide[31] and by heating 4-bromo-3,5-dinitrobenzaldehyde in methanolic sodium methoxide.[22a,32] The reaction of **13** with methyl thioglycolate and triethylamine in *N*,*N*-dimethylformamide gave the *tele* substitution product **16** in 52% yield, without any trace of the corresponding aldehyde.

Since the cyano group is somewhat less electron-withdrawing than the nitro group it was of interest to ascertain whether 3-trichloromethylbenzonitrile **18** would undergo *tele* nucleophilic substitution. Compound **18** was prepared by heating 3-cyanobenzoic acid in a mixture of phenylphosphonic dichloride and phosphorus pentachloride (Scheme 5). This is a general method given in a patent[18] where only the elemental analysis of the compound is given. One other method of preparing **18** is known, namely, photochlorination of 3-methylbenzonitrile.[33]

Heating compound **18** in methanol containing one equivalent of sodium methoxide afforded 5-dichloromethyl-2-methoxybenzonitrile **19**, a product of *tele* nucleophilic substitution. Surprisingly, the reaction of **18** with methyl thioglycolate and triethylamine afforded **20**, a product of a classical S_NAr reaction. To our knowledge this represents the first nucleophilic displacement of cyanide from a benzene derivative.



Scheme 4. Reagents: (a) $PhP(O)Cl_2$, PCl_5, 50°C, reflux; (b) MeONa, MeOH, room temperature; (c) $HSCH_2CO_2Me$, Et_3N, DMF, 120°C.



Scheme 5. Reagents: (a) $PhP(O)Cl_2$, PCl_5; (b) MeONa, MeOH, reflux; (c) $HSCH_2CO_2Me$, Et_3N, EtOH, reflux.

Reactions of compounds **2**, **13** and **18** with sodium phenoxide or thiophenol/triethylamine failed. Standard reactions with a variety of carbon and phosphorus nucleophiles and with sodium or potassium azide were also unsuccessful. In the above reactions starting material was recovered except for the reaction with azide which gave unrecognisable products.

Experimental

General methods

Melting points were taken on a Büchi 510 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 257 spectrometer, solids as Nujol mulls and liquids as thin films between sodium chloride discs. Elemental analyses were performed on a Carlo Erba 1106 elemental analyser. Nuclear magnetic resonance spectra were measured at 300 MHz on a Brüker AC 300 spectrometer or at 400 MHz on a Brüker AMX 400 spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained by use of Finnigan 4500 (low resolution) or JEOL JMS-AX 505W (high resolution) instruments using EI or CI (NH_3). Data are given for ions containing ^{35}Cl only. Appropriate isotope patterns were observed.

All reactions were carried out under argon. Analytical TLC was carried out on Fluka silica gel 60 F_{254}. Preparative flash chromatography was carried out using Merck 9385 silica gel. Light petroleum refers to the fraction with bp 40–60°C. Solvents and reagents were used as received from the manufacturers except for dichloromethane, ethanol, ethyl acetate, methanol and light petroleum that were dried and purified according to recommended procedures.[34]

1-Nitro-3-trichloromethylbenzene (2). A stirred mixture of 3-nitrobenzoic acid (1 g, 6 mmol) and phenylphosphonic dichloride (0.82 mL, 6.6 mmol) was warmed to 50°C. Phosphorus pentachloride (3.12 g, 15 mmol) was added portionwise with care while the mixture was thoroughly stirred. When about half of the phosphorus pentachloride was added and evolution of hydrogen chloride gas had subsided, the remainder of the phosphorus pentachloride was added in one portion and the mixture was heated under reflux for 15 h. The excess of phosphorus oxychloride was distilled off and the oily residue was poured slowly into a cold aqueous 10% sodium carbonate solution (45 mL) and then extracted with chloroform (3×15 mL) and dried (Na_2SO_4). The solvent was removed in vacuo and the residue was purified by flash chromatography (light petroleum) to give the *title compound* **2** (0.733 g, 50%) as a yellow oil (lit.[19a] bp 128°C/1 mmHg); ν_{max}(Nujol) 1530, 1350 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 7.60 (1 H, t, J=8.1 Hz, H-5), 8.16–8.24 (2 H, m, H-4 and H-6), 8.72 (1 H, s, H-2); *m*/*z* (EI) 239 (4, M^+), 204 (100), 158 (20), 122 (32), 73 (8%).

Reaction of 1-nitro-3-trichloromethylbenzene with methoxide. To a stirred solution of 1-nitro-3-trichloromethylbenzene (0.3 g, 1.2 mmol) in dry methanol (15 mL), was added a solution of sodium methoxide (0.067 g, 1.2 mmol) in dry methanol (5 mL). The mixture was heated under reflux for 24 h. The solvent was removed in vacuo and the residue purified by flash chromatography (8% ethyl acetate/light petroleum). Two fractions were obtained. The first fraction gave *4-methoxy-3-nitrobenzaldehyde* **6** (0.128 g, 59%) as pale yellow microcrystals, mp 82–84°C (lit.[22d] mp 81–83°C); ν_{max}(liquid film) 3100, 1535, 1350 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 4.04 (3 H, s, *Me*), 7.24 (1 H, d, J=7 Hz, H-5), 8.07 (1 H, d, J=7 Hz, H-6), 8.31 (1 H, s, H-2), 9.90 (1 H, s, C*H*O); *m*/*z* (EI) 181 (9, M^+), 150 (55), 135 (4), 104 (12), 78 (10); HRMS (EI): M^+ found 181.0368. $C_8H_7NO_4$ requires 181.0375. The second fraction gave *methyl 3-nitrobenzoate* **4** (0.05 g, 23%), identical to an authentic sample.

Reaction of 1-nitro-3-trichloromethylbenzene with methyl thioglycolate. *Method A:* To a stirred solution of 1-nitro-3-trichloromethylbenzene (0.3 g, 2 mmol) in dry methanol (20 mL) was added methyl thioglycolate (0.11 ml, 1.2 mmol) and triethylamine (0.25 mL, 1.8 mmol). The mixture was heated under reflux for 48 h. The solvent was removed in vacuo and the residue purified by flash chromatography (7% light petroleum/toluene). Two fractions were obtained. The first fraction gave *starting material* **2** (0.051 g, 18%). The second fraction gave *methyl (4-dichloromethyl-2-nitrophenylsulfanyl)acetate* **7** (0.12 g, 32%) as pale yellow oil; [Found: C, 38.72; H, 3.18; N,

4.19. $C_{10}H_9Cl_2NO_4S$ requires C, 38.84; H, 2.93; N, 4.53%]; ν_{max}(liquid film) 1740, 1510, 1355 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 3.76 (3 H, s, *Me*), 3.81 (2 H, s, CH_2), 6.74 (1 H, s, $CHCl_2$), 7.60 (1 H, dd, J=8.1, 4.7 Hz, H-6), 7.81 (1 H, d, J=8.1 Hz, H-5), 8.42 (1 H, s, H-3); δ_C (90 MHz, $CDCl_3$) 35.04, 53.03, 69.48, 123.93, 127.41, 129.58, 131.38, 137.87, 138.61, 168.94; *m/z* (EI) 309 (5, M^+), 274 (12), 195 (18), 150 (100), 84 (100), 76 (65%).

Method B: To a stirred solution of 1-nitro-3-trichloromethylbenzene (0.2 g, 0.8 mmol) and methyl thioglycolate (0.1 mL, 1 mmol) in dry methanol (15 mL) was added a solution of potassium carbonate (0.276 g, 2 mmol) in dry methanol (5 mL). The mixture was heated under reflux for 48 h. The solvent was evaporated under reduced pressure and to the residue water (15 mL) was added and the mixture extracted with dichloromethane (3×5 mL) and dried (Na_2SO_4). After removal of the solvent in vacuo the residue was purified by flash chromatography (7% light petroleum/toluene). Three fractions were obtained. The first fraction gave *starting material* **2** (0.048 g, 25%). The second fraction gave *methyl (4-dichloromethyl-2-nitrophenylsulfanyl)acetate* **7** (0.03 g, 12%), identical in all respects to compound **7** described in Method A. The third fraction gave *methyl (4-formyl-2-nitrophenylsulfanyl)acetate* **9** (0.13 g, 27%) as pale yellow oil; ν_{max}(liquid film) 1740, 1715, 1510, 1355 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.53 (3 H, s, *Me*), 3.70 (2 H, s, CH_2), 7.62 (1 H, dd, J=8.2, 4.8 Hz, H-6), 7.99 (1 H, d, J=8.2 Hz, H-5), 8.62 (1 H, d, J=4.8 Hz, H-3), 9.93 (1 H, s, C*H*O); *m/z* (CI, NH_3) 273 [100, $(M+NH_4)^+$], 252 (32), 228 (10), 178 (12%); HRMS (CI): $(M+NH_4)^+$, found 273.0542. $C_{10}H_{13}N_2O_5S$ requires 273.0544).

Method C: A mixture of 1-nitro-3-trichloromethylbenzene (0.3 g, 1.2 mmol), methyl thioglycolate (0.11 mL, 1.2 mmol) and triethylamine (0.25 mL, 1.8 mmol) in dry *N*,*N*-dimethylformamide (5 mL) and hexamethylphosphoric triamide (0.1 mL) under argon, was stirred at room temperature for 24 h. The mixture was poured onto ice-water (25 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography (7% light petroleum/toluene). Two fractions were obtained. The first fraction gave *starting material* **2** (0.054 g, 18%). The second fraction gave *methyl (4-dichloromethyl-2-nitrophenylsulfanyl)acetate* **7** (0.21 g, 67%), identical to compound **7** described in *Method A*.

4-Dimethoxymethyl-1-methoxy-2-nitrobenzene (10). To a stirred solution of methyl (4-dichloromethyl-2-nitrophenylsulfanyl)acetate (0.49 g, 1.6 mmol) in dry methanol (15 mL), was added sodium methoxide (0.43 g, 8 mmol). The mixture was heated under reflux for 10 h. The solvent was evaporated in vacuo and the residue was purified by flash chromatography (25% ethyl acetate/light petroleum) to give the *title compound* **10** (0.1 g, 28 %) as an oil; ν_{max}(liquid film) 1520, 1335 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.24 (6 H, s, OMe_2), 3.88 (3 H, s, O*Me*), 5.30 (1 H, s, C*H*), 7.20 (1 H, d, J=7.5 Hz, H-4), 7.85 (1 H, d, J=7.5 Hz, H-5), 8.46 (1 H, s, H-2); *m/z* (EI) 227 (37, M^+), 196 (100), 180 (14), 149 (46), 121 (75), 77 (28%); HRMS (EI): M^+, found 227.0820. $C_{10}H_{13}NO_5$ requires 227.0794.

3-Oxo-3,4-dihydro-2*H*-1,4-benzothiazine-6-carboxaldehyde (11). Zinc powder (0.56 g, 9 mmol) was added portionwise to a stirred solution of methyl (4-dichloromethyl-2-nitrophenylsulfanyl)acetate (0.2 g, 0.6 mmol) and calcium chloride (0.1 g, 0.9 mmol) in 80% aqueous methanol (15 mL). The suspension was heated under reflux for 2 h, cooled to room temperature and filtered. The filtrate was diluted with water (15 mL) and extracted with chloroform (3×10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography (8% ethyl acetate/light petroleum). Two fractions were obtained. The first fraction gave *starting material* **7** (0.03 g, 16%). The second fraction gave the *title compound* **11** (0.065 g, 52%) as a yellow oil; ν_{max}(liquid film) 3210, 1705, 1665 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.71 (2 H, s, CH_2), 4.66 (1 H, s, N*H*), 7.49 (1 H, d, J=7.2 Hz, H-8), 7.57 (1 H, d, J=7.2 Hz, H-7), 7.91 (1 H, s, H-5), 9.98 (1 H, s, C*H*O); *m/z* (EI) 193 (76, M^+), 164 (68), 136 (42), 69 (100), 45 (59%); HRMS (EI): M^+, found 193.0192. $C_9H_7NO_2S$ requires 193.0197.

1,3-Dinitro-5-trichloromethylbenzene (13). A stirred mixture of 3,5-dinitrobenzoic acid (5 g, 24 mmol) and phenylphosphonic dichloride (3.7 mL, 26 mmol) was warmed to 50°C. Phosphorus pentachloride (12.5 g, 60 mmol) was added portionwise with care over 1 h while the mixture was thoroughly stirred. Evolution of hydrogen chloride gas occurred throughout the addition. The resulting solution was heated under reflux for 15 h, and then phosphorus oxychloride was distilled off. The oily residue was poured into 20% aqueous sodium carbonate (200 mL) and the mixture was extracted with chloroform (3×40 mL) and dried (Na_2SO_4). The solvent was removed in vacuo and the residue was recrystallised from *N*,*N*-dimethylformamide and water to give the *title compound* **13** (4.56 g, 75%) as pale yellow needles, mp 76–77°C (lit.[29] mp 76.5–77.5°C); ν_{max}(Nujol) 1515, 1350 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 9.13 (2 H, s, H-4, H-6), 9.25 (1 H, s, H-2); *m/z* (EI) 284 (25, M^+), 249 (100), 233 (40), 199 (10), 183 (35), 167 (36), 143 (44), 107 (42), 72 (20%).

4-Methoxy-3,5-dinitrobenzaldehyde (15). To a stirred solution of 1,3-dinitro-5-trichloromethylbenzene (0.3 g, 1.2 mmol) in dry methanol (15 mL), was added a solution of sodium methoxide (0.071 g, 13 mmol) in dry methanol (5 mL). Stirring was continued for 24 h at room temperature and then the solvent was removed in vacuo. The residue was purified by flash chromatography (8% ethyl acetate/light petroleum) to give the *title compound* **15** (0.15 g, 55%) as colourless needles, mp 86–87°C (lit.[32] mp 87°C); [Found: C, 42.53; H, 2.88; N, 11.34. $C_8H_6N_2O_6$ requires C, 42.50; H, 2.70; N, 11.42%]; ν_{max}(Nujol) 1690, 1550, 1370 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.99 (3 H, s, *Me*), 9.10 (2 H, d, J=2.1 Hz, H-2 and H-6); 9.20 (1 H, t, J=2.1 Hz, C*H*O); *m/z* (CI, NH_3) 278 [100, $(M+NH_4+2NH_3)^+$], 218 (12), 167 (5), 148 (10), 134 (39), 108 (15), 78 (10%).

Reaction of 1,3-dinitro-5-trichloromethylbenzene with methyl thioglycolate. To a stirred solution of 1,3-dinitro-5-trichloromethylbenzene (0.3 g, 1.2 mmol) and methyl thioglycolate (0.1 ml, 1.3 mmol) in dry *N*,*N*-dimethylformamide (15 mL), was added dropwise a solution of triethylamine (0.3 mL, 2 mmol) in dry *N*,*N*-dimethylformamide

(5 mL). The resulting mixture was heated at 120°C for 10 h after which it was cooled to 0°C. Water (50 mL) was added and the mixture extracted with ethyl acetate (3×15 mL) and diethyl ether (3×15 mL). The combined extracts were dried (Na_2SO_4) and the solvents evaporated. The residue was purified by flash chromatography (25% ethyl acetate/light petroleum) to give *starting material* **13** (0.06 g, 20%) and *methyl (4-dichloromethyl-2,6-dinitrophenylsulfanyl)acetate* **16** (0.22 g, 52%) as a yellow oil; [Found: C, 33.72; H, 2.19; N, 7.94. $C_{10}H_8Cl_2N_2O_6S$ requires C, 33.90; H, 2.28; N, 7.91%]; ν_{max}(liquid film) 1740, 1550, 1370 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.72 (3 H, s, *Me*), 3.81 (2 H, s, C*H*$_2$), 6.76 (1 H, s, C*H*Cl_2), 9.13 (2 H, s, H-4, H-6); *m*/*z* (EI) 355 (15, MH^+), 329 (38), 307 (100), 289 (73), 256 (18), 210 (35%).

3-Trichloromethylbenzonitrile (18). A mixture of 3-cyanobenzoic acid, (5 g, 34 mmol) and phenylphosphonic dichloride (10.2 mL, 68 mmol) was heated to 60°C and stirred as phosphorus pentachloride (25 g, 115 mmol) was added in portions until evolution of hydrogen chloride slowed and the mixture became clear. The remainder of the phosphorus pentachloride was then added in a single portion and the mixture was heated under reflux for 16 h. The excess of phosphorus oxychloride was distilled off and the oily residue was poured slowly onto crushed ice (300 mL). The resulting mixture was neutralised with potassium carbonate and then extracted with chloroform (3×100 mL). The combined extracts were dried ($MgSO_4$), the solvent was evaporated, and the residue was distilled at 155°C/6 mmHg to give the *title compound* **18** (6.8 g, 91%) as a colourless oil (lit.[33a] bp 74–76°C/0.1 mmHg); ν_{max}(Nujol) 2180 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.56 (1 H, t, *J*=8 Hz, H-5), 7.67 (1 H, d, *J*=8 Hz, H-6), 8.13 (1 H, d, *J*=8 Hz, H-4), 8.17 (1 H, s, H-2); *m*/*z* (CI) 220 (80, MH^+), 184 (100), 114 (45%).

5-Dimethoxymethyl-2-methoxybenzonitrile (19). Sodium (1.0 g, 45 mmol) was dissolved in dry methanol (30 mL) and kept over 4 Å molecular sieves. 3-Trichloromethylbenzonitrile (2.0 g, 9 mmol) was added, and the mixture was heated under reflux for 22 h. The reaction mixture was filtered and water (100 mL) was added to the filtrate. The resulting solution was extracted with chloroform (3× 50 mL), and the combined extracts were dried ($MgSO_4$) and the solvents were evaporated. Purification of the crude product by flash chromatography (50% ethyl acetate/light petroleum) gave the *title compound* **19** (1.01 g, 54%) as a colourless oil; ν_{max}(liquid film) 2180 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 3.30 (6 H, s, O*Me*$_2$), 3.90 (3 H, s, O*Me*), 5.30 (1 H, s, C*H*), 6.95 (1 H, d, *J*=9 Hz, H-3), 7.55 (1 H, d, *J*=9 Hz, H-4), 7.60 (1 H, s, H-6); *m*/*z* (EI) 207 (4, M^+), 176 (100), 160 (3),75 (3%); HRMS (EI): M^+, found 207.0893 $C_{11}H_{13}NO_3$ requires 207.0895.

Methyl (3-trichloromethylphenylsulfanyl)acetate (20). To a stirred solution of 3-trichloromethylbenzonitrile (0.3 g, 1.3 mmol) and methyl thioglycolate (0.16 mL, 1.4 mmol) in dry ethanol (15 mL), was added dropwise a solution of triethylamine (0.31 mL, 2.25 mmol) in dry ethanol (5 mL). The mixture was heated under reflux for 10 h. The solvent was removed in vacuo and the residue was purified by flash chromatography (12% ethyl acetate/light petroleum) to give the *title compound* **20** (0.116 g, 30%) as a colourless oil; [Found: C, 39.97; H, 3.29. $C_{10}H_9Cl_3O_2S$ requires C, 40.28; H, 3.04%]; ν_{max}(liquid film) 1740 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.52 (3 H, s, *Me*), 3.68 (2 H, s, C*H*$_2$), 7.54 (1 H, t, *J*=7.9 Hz, H-5), 7.65 (1 H, d, *J*=7.9 Hz, H-4), 8.09 (1 H, d, *J*=7.9 Hz, H-6), 8.15 (1 H, s, H-2); δ_C (90 MHz, $CDCl_3$) 41, 52, 67, 112, 117, 129, 129, 129, 133, 145, 169; *m*/*z* (EI) 298 (5, M^+), 268 (42), 219 (15), 184 (100), 114 (30%).

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