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Synthesis of Dinitroaniline as Plant Growth Regulators and for Identification of Amines

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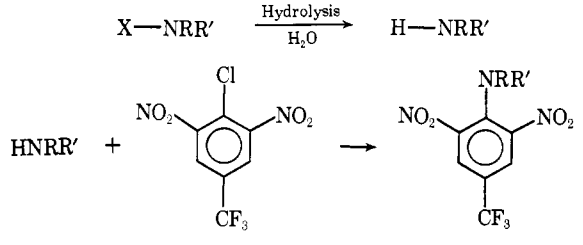
The synthesis of systematic series of 4-substituted amino-3,5-dinitrobenzotrifluorides and 4-substituted 2,6-dinitro-*N*,*N*-di-*n*-propylanilines is reported. The anilines formed by the reaction of 4-substituted 2,6-dinitrochlorobenzenes with amines liberated by the hydrolysis of carbamate, urea, and amide pesticides can be used for the gas chromatographic determination of these pesticides. The preparative procedures developed can be extended to other series of dinitroanilines.

Although the dinitroanilines have been recognized as effective preemergence herbicides for approximately 10 years (Pieczarka *et al.*, 1961, 1962a,b), mode of action studies (Amato *et al.*, 1965; Mann *et al.*, 1968; Standifer *et al.*, 1965; Talbert, 1965; Negi *et al.*, 1968; Shultz *et al.*, 1968; Sawamura and Jackson, 1968a,b) have been limited to the commercially available trifluralin (α,α,α-trifluoro-2,6-dinitro-*N*,*N*-di-*n*-propyl-*p*-toluidine) and nitralin (4-methylsulfonyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline). Structure–activity studies (Gentner, 1966, 1970) of the dinitroanilines have also been limited to simple alkyl analogs of trifluralin and nitralin.

Recently, Crosby and Bowers (1968) reported a simple and sensitive procedure for the analysis of pesticides containing the amine function. In this procedure, carbamate, urea, amide, and other amine-containing pesticides are hydrolyzed, and the amine, which is liberated, is analyzed as a dinitroaniline or other similar derivative. The most suitable derivatives were mono- and dinitro-α,α,α-trifluoro-*p*-toluidines; however, the gas chromatographic behavior of only a very limited number



of these derivatives had been studied.

The synthesis of systematic series of 4-substituted amino-3,5-dinitrobenzotrifluorides and 4-substituted 2,6-dinitro-*N*,*N*-di-*n*-propylanilines is presented. The wide variety of steric, electronic, and hydrophobic factors present in these series enable the physical and biochemical properties of the dinitroanilines to be fully investigated.

EXPERIMENTAL

General Procedures for Preparing 4-Substituted 2,6-Dinitrobenzenes. The two general procedures for synthesizing 4-substituted 2,6-dinitrochlorobenzenes (the "direct" nitration of 4-substituted chlorobenzenes and the "indirect" nitration of 4-substituted phenols and subsequent chlorodehydroxylation of the dinitrophenol) are exemplified by the specific preparations below.

4-Chloro-3,5-dinitrobenzotrifluoride. METHOD A. To a mixture of 200 ml of fuming sulfuric acid (30–33%) and 180 ml of red fuming nitric acid at 60°C was added dropwise with stirring 50 g of 4-chloro-3-nitrobenzotrifluoride (Aldrich Chemical Co.) over a period of 30 min. The mixture was kept at 60°C for an additional 30 min and then slowly raised to 100–105°C over a period of 45 min. It was kept at this temperature for 1.5 hr, and after having been cooled to room temperature, was poured over cracked ice and allowed to sit overnight. The mixture was then filtered, and the precipitate was dissolved in ether and rinsed several times with distilled water. The solvent ether was removed at room temperature and the residue recrystallized from ethyl alcohol. The yield of 4-chloro-3,5-dinitrobenzotrifluoride was 74% (45 g), a pale yellow crystalline compound which melted at 56–58°C (Soper, 1966; 53–57°C).

4-*tert*-Butyl-2,6-dinitrochlorobenzene. METHOD B. A solution of 25 g of 4-*tert*-butylphenol (Aldrich Chemical Co.) in 100 ml of glacial acetic acid was added dropwise with stirring over a period of 45 min to a mixture of 50 ml of concentrated nitric acid and 75 ml of glacial acetic acid at 5°C (Dutton *et al.*, 1953a). The reaction mixture was then allowed to warm to room temperature for 30 min. The reaction was then terminated by pouring the mixture over cracked ice. 4-*tert*-Butyl-2,6-dinitrophenol precipitated and was filtered off cold. The crude phenol can be purified as the piperidine salt (recrystallized from 95% ethyl alcohol), and the pure phenol liberated by acidifying the salt in water and extracting

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with benzene [this method of purification is recommended rather than vacuum distillation (Dutton *et al.*, 1953b) because a similar compound, 4-ethyl-2,6-dinitrophenol, exploded violently in a careful attempt to distil it]. The yield of crude phenol was 85% (34 g), melting at 91–93°C, and the yield of pure phenol 50% (19.7 g), melting at 93.5–94°C (Cullinane and Leyshon, 1954; 94°C).

4-*tert*-Butyl-2,6-dinitrophenol (crude) was converted to 4-*tert*-butyl-2,6-dinitrochlorobenzene by dissolving 20 g of the phenol in a mixture of 200 ml of phosphorus oxychloride and 35 ml of dimethylformamide (DMF) contained in a 1-l. round-bottomed flask equipped with a reflux condenser and drying tube. The DMF was added to the phosphorus oxychloride at 10–20°C. The mixture was heated on a steam cone for 18 hr, and the resultant dark brown solution, after cooling to room temperature, poured on a large excess of cracked ice (usually a 3-l. beaker of ice is sufficient). After hydrolysis was complete, the precipitated 4-*tert*-butyl-2,6-dinitrochlorobenzene was collected by filtration. The crude product was purified by dissolving it in 75 ml of benzene, washing twice with 6 *N* sulfuric acid, and washing repeatedly with 10% sodium carbonate until the aqueous wash was nearly colorless. The benzene solution was dried ($MgSO_4$) and passed through an activated alumina column (Woelm W200 neutral). A little additional benzene was used to complete elution. The solvent was allowed to evaporate at room temperature and the residue recrystallized from hexane. The yield of 4-*tert*-butyl-2,6-dinitrochlorobenzene, melting at 115–117°C (Boedtker, 1906; 116–117°C) was 72% (15.5 g).

METHOD B′. 4-*tert*-Butyl-2,6-dinitrophenol (20 g) was converted to 4-*tert*-butyl-2,6-dinitrochlorobenzene by heating it with a mixture of 35 ml of benzenesulfonyl chloride and 80 ml of *N*,*N*-diethylaniline in a sealed tube at 100°C for 20 hr. The resultant dark blue tar was dissolved in benzene and washed twice with 6 *N* sulfuric acid to remove unreacted *N*,*N*-diethylaniline. The unreacted phenol was removed by washing the benzene solution with 10% sodium carbonate until the aqueous wash was colorless. The solution was dried ($MgSO_4$) and passed through an activated alumina column (Woelm W200 neutral). The benzene was removed at room temperature under vacuum, and 4-*tert*-butyl-2,6-dinitrochlorobenzene isolated from the oily residue by recrystallization from methyl alcohol–water (Hawthorne and Cram, 1952). A further crop of crystals was obtained by diluting the methyl alcohol with water, extracting with ether, and evaporating the ether. The oily residue was diluted with a little acetone and cooled to Dry Ice–acetone temperature, at which time a solid residue separated. The residue was rapidly filtered under vacuum before it could warm. The two crops of product were combined and recrystallized from hexane. 4-*tert*-Butyl-2,6-dinitrochlorobenzene, melting at 114–116°C, was obtained in a yield of 48% (10.4 g).

4-Chloro-3,5-dinitrobenzoic Acid. METHOD C. A mixture of 100 g of 4-chlorobenzoic acid (Aldrich Chemical Co.), 250 g of nitric acid (d 1.5), and 400 g of concentrated sulfuric acid was slowly heated to 95–100°C on a steam cone. The reaction mixture was maintained at this temperature for 4 hr and then cooled to room temperature and quenched by pouring over cracked ice. The cold solution was then filtered and the precipitate, 4-chloro-3,5-dinitrobenzoic acid, recrystallized from methyl alcohol. The yield of 4-chloro-3,5-dinitrobenzoic acid, melting at 160–162°C (Berkenheim and Lur'e, 1936; 161–163°C), was 78% (123 g).

METHOD C′. To a mixture of 60 ml of 90% nitric acid, 50 ml of concentrated nitric acid and 280 ml of glacial acetic acid was added, in small portions, 50 g of 4-hydroxybenzoic acid (Aldrich Chemical Co.) at room temperature, with stirring. The reaction mixture was allowed to stand at room temperature for 4 hr and then poured over cracked ice. After standing for 2 hr, the precipitate was filtered off and dried at room temperature for 48 hr. The yield of 4-hydroxy-3,5-dinitrobenzoic acid, melting at 240–244°C (Van Alphen, 1930; 243°C), was 62% (51 g).

4-Hydroxy-3,5-dinitrobenzoic acid (without further purification) was converted to 4-chloro-3,5-dinitrobenzoic acid by heating 50 g of the phenol in a 1-l. round-bottomed flask (equipped with a reflux condenser and drying tube), containing a mixture of 200 ml of phosphorus oxychloride and 15 ml of DMF, on a steam cone for 4 hr. The mixture was then cooled and the reaction quenched by pouring over a large excess of cracked ice. After hydrolysis of the phosphorus oxychloride was complete, the product was isolated by filtration and rinsed with a little cold water. The yield of 4-chloro-3,5-dinitrobenzoic acid, melting at 160–163°C (from ethyl alcohol), was 76% (38 g).

4-Phenyl-2,6-dinitrochlorobenzene. METHOD D. To 25 g of 4-phenylphenol (Aldrich Chemical Co.) in 25 ml of glacial acetic acid was added dropwise with stirring a mixture of 25 ml of concentrated nitric acid and 75 ml of glacial acetic acid during a period of 30 min. The reaction was maintained at 0–5°C. Water (200 ml) was then added and the precipitate filtered. The filter cake was rinsed with approximately 50 ml of water and then recrystallized from ethyl alcohol. The yield of product, melting at 150–152°C (Jones and Chapman, 1952; 151–152°C), was 75% (28.6 g).

4-Phenyl-2,6-dinitrophenol was converted to 4-phenyl-2,6-dinitrochlorobenzene by heating 4 g of the phenol with a mixture of 15 ml of phosphorus oxychloride and 2 ml of DMF contained in a 50-ml round-bottomed flask (equipped with a reflux condenser and drying tube) on a steam cone for 2.0 hr. The mixture was then cooled to room temperature and the reaction quenched by pouring over cracked ice. The product, which precipitated, was isolated, dissolved in benzene, and washed several times with 10% sodium carbonate. The benzene was allowed to evaporate and the residue recrystallized from hexane. The yield of 4-phenyl-2,6-dinitrochlorobenzene, melting at 155–156°C (Bunnett *et al.*, 1954; 155–156°C), was 72% (3.1 g).

4-(4′-Nitrophenyl)-2,6-dinitrochlorobenzene. METHOD E. To a mixture of 250 ml of glacial acetic acid and 40 ml of fuming nitric acid (d 1.52) was added 25 g of 4-phenylphenol, at room temperature and with stirring, over a period of 1.5 hr. The reaction mixture was allowed to sit at room temperature for an additional 2 hr, and was then poured over cracked ice. The solution was filtered and the precipitate washed with cold water and then dissolved in 500 ml of boiling water. Upon cooling, crystals of 4-(4′-nitrophenyl)-2,6-dinitrophenol were deposited in a yield of 69% (31 g), melting at 195–196°C (Jones and Chapman, 1952; 197–198°C).

4-(4′-Nitrophenyl)-2,6-dinitrophenol was converted to 4-(4′-nitrophenol)-2,6-dinitrochlorobenzene by heating 12 g of the phenol with a mixture of 35 ml of phosphorus oxychloride and 4 ml of DMF on a steam cone for 45 min. The reaction was then quenched by pouring over cracked ice, and the product, which precipitated, recrystallized from acetone. The yield of 4-(4′-nitrophenyl)-2,6-dinitrochlorobenzene, melting at 175–176°C (Sen, 1945; 171°C) was 81% (10.3 g).

2,4,6-Trinitrochlorobenzene. METHOD F. A mixture of 20 g of 2,4,6-trinitrophenol (picric acid), 100 ml of phosphorus oxychloride, and 15 ml of DMF (contained in a 250-ml

round-bottomed flask fitted with a reflux condenser and drying tube) was heated on a steam cone for 30 min. The reaction was then quenched by pouring over cracked ice, and the resultant precipitate filtered off. The product was purified by recrystallization from hexane–ether. The yield of 2,4,6-trinitrochlorobenzene (picryl chloride), melting at 83–84°C (Hertel, 1933; 83°C), was 90% (19.5 g).

4-Methoxy-2,6-dinitrochlorobenzene. METHOD G. To 425 ml of nitric acid (d 1.4) was rapidly added 100 g of 4-methoxy-2-nitroaniline, with stirring. The temperature was maintained at 30–35°C for an hour by occasional outside cooling. During this time red crystals of product separated. The reaction mixture was cooled to approximately 0°C, filtered, the precipitate washed with 15% nitric acid, and then washed several times with cool water. The yield of 4-methoxy-2,6-dinitroaniline, which was pure as obtained, melting at 160–162°C (Elderfield *et al.*, 1946; 161–163°C) was 55% (70 g).

4-Methoxy-2,6-dinitroaniline was converted to 4-methoxy-2,6-dinitrochlorobenzene by the Sandmeyer reaction. To a solution of 5 g (0.023 mol) of 4-methoxy-2,6-dinitroaniline in 25 ml of concentrated sulfuric acid was added, in small portions, 2 g (0.029 mol) of sodium nitrite at 10°C. The solution was then treated slowly at room temperature with a mixture of 2.5 g of cupric sulfate, 1.25 g of sodium chloride, 5 ml of water, 1.25 g of copper filings, and 10 ml of concentrated hydrochloric acid, and heated on a steam bath for approximately 1.5 hr. The mixture was then cooled, diluted with 100 ml of cold water, and extracted with benzene. The benzene solution was repeatedly washed with 10% sodium carbonate until the aqueous wash was nearly colorless. It was then dried ($MgSO_4$) and passed through an activated alumina column (Woelm W200 neutral). A little additional benzene was used to complete elution. Evaporation of the benzene left 4-methoxy-2,6-dinitrochlorobenzene, which was further purified by recrystallization from hexane. The yield of product, melting at 122–123°C (Leandri and Tundo, 1954; 123°C), was 32% (1.7 g).

Other 4-Substituted 2,6-Dinitrochlorobenzenes. 4-Methyl-2,6-dinitrochlorobenzene, 4-ethyl-2,6-dinitrochlorobenzene, 4-*n*-propyl-2,6-dinitrochlorobenzene, 4-iso-propyl-2,6-dinitrochlorobenzene, 4-*n*-butyl-2,6-dinitrochlorobenzene, and 4-*sec*-butyl-2,6-dinitrochlorobenzene were synthesized from the corresponding 4-alkyl-2,6-dinitrophenols by Method B in yields of 70–80%. 4-Bromo-2,6-dinitrochlorobenzene and 4-chloro-2,6-dinitrochlorobenzene were also synthesized from the corresponding dinitrophenols by Method B, except that the chlorination time was 4 hr. These compounds were obtained in yields of 54 and 85%, respectively. 2,6-Dinitrochlorobenzene and 4-cyano-2,6-dinitrochlorobenzene were purchased from Aldrich Chemical Co. and used without further purification.

4-*n*-Butylphenol (Dutton *et al.*, 1953b). To 103 g (1.1 mol) of phenol in 75 ml of benzene was added 132 g (1.25 mol) of butyryl chloride. The reaction mixture was heated on a steam cone for 45 min and then distilled. The fraction boiling at 190–195°C was collected and redistilled to give 160 g (80%) of phenylbutyrate, boiling at 192–193°C.

To 50 g of aluminum chloride in a three-necked 2-l. flask heated to 70°C was rapidly added, with stirring, 140 g of phenylbutyrate heated to 50°C. The reaction mixture rose to approximately 100°C and was then rapidly heated to 140–145°C and maintained at this temperature for 1 hr. The mixture was then cooled to room temperature and hydrolyzed by adding 2.0 l. of ice cold 6 *N* hydrochloric acid. The oil which separated was washed with dilute hydrochloric acid, dried, and distilled. 4-Hydroxybutyrophenone was separated from the 2 isomer by collecting the fraction boiling at 165°C at 1.0 mm.

4-Hydroxybutyrophenone was reduced to 4-*n*-butylphenol by the Martin modification (Martin, 1936) of the Clemmensen method (Adams, 1952; Clemmensen, 1914). A mixture of 100 g of mossy zinc, 10 g of mercuric chloride, 5 ml of concentrated hydrochloric acid, and 150 ml of water was shaken for 5 min. The solution was decanted and 75 ml of water, 175 ml of concentrated hydrochloric acid, 100 ml of toluene, 2 ml of acetic acid, and 50 g of 4-hydroxybutyrophenone were added to the residue. The reaction mixture was refluxed for 24 hr with three 50-ml portions of concentrated hydrochloric acid added at intervals of 6 hr. The mixture was then cooled and the organic phase distilled. 4-*n*-Butylphenol was collected as the fraction, distilling at 90°C (1 mm) in a yield of 61% (28 g).

General Procedure for Preparing N-Substituted 2,6-Dinitro-4-substituted Anilines. The two general procedures used for synthesizing N-substituted 2,6-dinitro-4-substituted anilines (aminodechlorination of the appropriate 4-substituted 2,6-dinitrochlorobenzene, and modification of the substituent in 4-substituted 2,6-dinitro-*N*,*N*-di-*n*-propylanilines) are exemplified by the specific preparations below.

4-Chloro-2,6-dinitro-*N*,*N*-di-*n*-propylaniline. METHOD H. A mixture of 10 g (0.042 mol) of 2,6-dinitro-1,4-dichlorobenzene and 8.5 g (0.084 mol) of di-*n*-propylamine in 25 ml of absolute alcohol was heated in a sealed tube for 4 hr at 85–95°C. The tube was cooled and its contents were dissolved in 100 ml of hexane. The hexane solution was washed several times with dilute sulfuric acid and then several times with 10% sodium carbonate. The hexane solution was then dried ($MgSO_4$) and passed through an activated alumina column (Woelm W200 neutral). Additional hexane was used to complete elution. The solvent was evaporated and the residue recrystallized from 95% ethyl alcohol. 4-Chloro-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, a reddish-orange crystalline compound, melting at 70–71°C (Soper, 1966; 71°C), was produced in a yield of 86% (10.9 g).

2,4,6-Trinitro-*N*,*N*-di-*n*-propylaniline. METHOD I. Ten grams (0.04 mol) of 2,4,6-trinitrochlorobenzene was dissolved in a minimal amount of acetone and diluted with 50 ml of absolute ethyl alcohol. To this solution was added (dropwise and with stirring) at room temperature 8.1 g (0.08 mol) of di-*n*-propylamine. During this time an orange precipitate formed. The solution was diluted with 100 ml of water and filtered. The precipitate was dissolved in 1:1 ether–benzene and washed twice with 5% sodium bicarbonate. Evaporation of the solvent and recrystallization of the residue from methyl alcohol afforded 2,4,6-trinitro-*N*,*N*-di-*n*-propylaniline, melting at 138–139°C (Hollemann, 1930; 38°C) in 90% yield (10.2 g).

4-Diisopropylamino-3,5-dinitrobenzotrifluoride. METHOD J. A mixture of 20 g of 4-chloro-3,5-dinitrobenzotrifluoride, 35 ml of diisopropylamine, and 100 ml of benzene was heated in a sealed tube at 85–95°C for 96 hr. The tube was cooled and its contents were mixed with an excess of dilute sulfuric acid. The aqueous layer which separated was discarded and the remaining benzene layer washed with dilute sulfuric acid until the aqueous wash was colorless. The benzene solution was then repeatedly washed with dilute 10% sodium carbonate until the wash was colorless. The organic phase was dried ($MgSO_4$) and passed through an activated alumina column (Woelm W200 neutral) and eluted with a little additional benzene. The solvent was distilled under vacuum (aspirator) and the residual red oil dissolved in approximately 20 ml of

hexane. The hexane solution was cooled to −5°C for several hours, whereupon crystals of unreacted 4-chloro-3,5-dinitrobenzotrifluoride separated and were removed by rapid filtration. This process was repeated, gradually lowering the temperature to −45°C, until no more starting material was obtained. The hexane solution was diluted with approximately 20 ml of additional hexane and passed through an activated alumina column. The hexane solution was then washed twice with 25 ml of 0.5% ethanolamine, dried ($MgSO_4$), and passed through an activated alumina column. The solvent was evaporated under vacuum (aspirator) leaving 4-diisopropylamino-3,5-dinitrobenzotrifluoride as a red viscous oil in a yield of 5–7%.

4-*n*-Propylamino-3,5-dinitrobenzotrifluoride. METHOD K. To a solution of 5 g (0.019 mol) of 4-chloro-3,5-dinitrobenzotrifluoride in 25 ml of absolute ethyl alcohol was added dropwise, with stirring, 2.2 g (0.038 mol) of *n*-propylamine. The solution was then heated to boiling on a steam bath for 15 min. It was then dissolved in two volumes of hexane and washed twice with dilute sulfuric acid, and then washed repeatedly with 10% sodium carbonate until the wash was nearly colorless. The solution was dried and passed through an activated alumina column and eluted with a little additional hexane. The solvent was then evaporated and the residue recrystallized from ethyl alcohol. The yield of 4-*n*-propylamino-3,5-dinitrobenzotrifluoride, melting at 55–58°C, was 81% (4.4 g).

4-Dimethylcarbamyl-2,6-dinitro-*N*-*N*-di-*n*-propylaniline. METHOD L. To a solution of 20 g (0.063 mol) of 4-chloro-3,5-dinitrobenzoic acid dissolved in 125 ml of absolute ethyl alcohol was added dropwise, with stirring, 19.2 g (0.19 mol) of dipropylamine. The reaction mixture was heated to refluxing temperatures for approximately 1.5 hr and then cooled to room temperature. The mixture was then added to an excess of dilute hydrochloric acid containing a little cracked ice, whereupon 4-carboxy-2,6-dinitro-*N*-*N*-di-*n*-propylaniline separated as an orange crystalline solid. The solution was filtered and the product dried at room temperature for a week. The yeild of 4-carboxy-2,6-dinitro-*N*-*N*-di-*n*-propylaniline, melting at 96–100°C (Soper, 1966; 95–100°C), was 89% (22.8 g).

4-Carboxy-2,6-dinitro-*N*-*N*-di-*n*-propylaniline was converted to 4-dimethylcarbamyl-2,6-dinitro-*N*-*N*-di-*n*-propylaniline by adding 7.7 g (0.035 mol) of phosphorus pentachloride in small portions to 10 g (0.032 mol) of the acid in 50 ml of benzene. The reaction mixture was allowed to stand at room temperature for 30 min and then warmed to 50°C and maintained at this temperature for an additional 30 min. The benzene was removed under vacuum and 100 ml of hexane added. The hexane was brought to boiling and then cooled to room temperature and the solvent decanted. The residual 3,5-dinitro-4-*N*,*N*-di-*n*-propylaminobenzoyl chloride was dissolved in a minimal amount of benzene and added with rapid stirring to a large excess of 40% aqueous dimethylamine. The temperature during addition was kept below 20°C. The solution was acidified with hydrochloric acid and then extracted twice with 75 ml of diethyl ether. The extracts were combined and washed three times with 10% sodium carbonate. Evaporation of the ether afforded 6.2 g (57%) of 4-dimethylcarbamyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, melting at 118–119°C (Soper, 1966; 117–119°C).

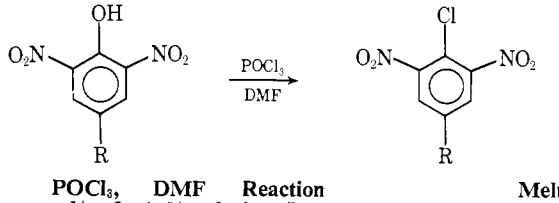
4-Amino-2,6-dinitro-*N*,*N*-di-*n*-propylaniline. METHOD M. 3,5-Dinitro-4-*N*,*N*-di-*n*-propylaminobenzoyl chloride, synthesized from 10 g of the corresponding acid as in Method L, was dissolved in 50 ml of glacial acetic acid. To this solution was added 2.3 g of sodium azide in small portions over a period of 30 min. The reaction mixture was warmed to approximately 60°C for several minutes and then allowed to sit for an hour at room temperature. It was then added to approximately 300 ml of ice water, and the aqueous solution extracted twice with 75 ml of diethyl ether. The extracts were combined and washed twice with 50 ml of 5% sodium bicarbonate. Evaporation of the ether afforded 5.0 g (49%) of 4-carboxyazido-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, melting at 100–103°C.

To 50 ml of concentrated sulfuric acid was added 5 g of 4-carboxyazido-2,6-dinitro-*N*,*N*-di-*n*-propylaniline in small portions. The reaction mixture was then heated on a steam cone for 45 min, whereupon nitrogen was evolved. After cooling to room temperature, the reaction was quenched by pouring over cracked ice. The solution was extracted twice with 50 ml of carbon tetrachloride, and the extracts were combined and washed several times with 10% sodium carbonate until the wash was colorless. Evaporation of the carbon tetrachloride and recrystallization of the residue from hexane yielded 1.6 g (35%) of 4-amino-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, melting at 84–85°C.

Other 4-Substituted 2,6-Dinitro-*N*,*N*-di-*n*-propylanilines. 4-Methoxy-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-methyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-ethyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-*n*-propyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-isopropyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-*n*-butyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-*sec*-butyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-*tert*-butyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-phenyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-(4′-nitrophenyl)-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-fluoro-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-bromo-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, and 4-cyano-2,6-dinitro-*N*,*N*-di-*n*-propylaniline were synthesized from the corresponding 4-substituted 2,6-dinitrochlorobenzenes and di-*n*-propylamine by Method H in 60–90% yield.

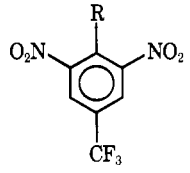
4-Carbamyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-diethylcarbamyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, 4-di-*n*-propylcarbamyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline, and 4-di-isopropylcarbamyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline were syn-

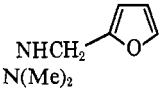
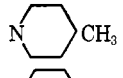
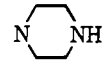
Table I. Conversion of 4-Substituted 2,6-Dinitrophenols to 4-Substituted 2,6-Dinitrochlorobenzenes by Phosphorus Oxychloride



R	$POCl_3$, ml/g of phenol	DMF (ml/g of phenol)	Reaction time (hr at 90–95°C)	Yield, %	Melting point, °C
NO_2	10	0.5	0.3	92	83–84
COOH	15	0.5	3.7	79	160–163
Cl	15	1	7	85	104–105
F	15	2	14	73	71–72
Me	15	5	20	70	117–118
Et	15	5	20	74	79–80
n-Pr	15	5	20	75	54–55
i-Pr	15	5	20	72	61–62
n-Bu	15	5	20	73	63–64
sec-Bu	15	5	20	72	60–61
tert-Bu	15	5	20	76	115–116
OCH_3	15	5	20	No reaction	

Table II. Physical Properties of 4-Substituted 3,5-Dinitrobenzotrifluorides



R	Melting point, °C		Elemental composition	Molecular weight[a]	
	Observed	Reported		Required	Found
NH_2	142–144	143–144[b]	$C_7H_4F_3N_3O_4$		
NH(Me)	87–89		$C_8H_6F_3N_3O_4$	265.03097	265.03001
NH(Et)	69–73	70–73[c]	$C_9H_8F_3N_3O_4$	279.04661	279.04582
NH(*n*-Pr)	55–58		$C_{10}H_{10}F_3N_3O_4$	293.06225	293.06297
NH(*iso*-Pr)	63–65		$C_{10}H_{10}F_3N_3O_4$	293.06225	293.06268
NH(*n*-Bu)	Oil		$C_{11}H_{12}F_3N_3O_4$	307.07789	307.07885
NH(*sec*-Bu)	71–72	69–71[d]	$C_{11}H_{12}F_3N_3O_4$		
NH(*i*-Bu)	65–66		$C_{11}H_{12}F_3N_3O_4$	307.07789	307.07915
NH(*tert*-Bu)	54–55		$C_{11}H_{12}F_3N_3O_4$	307.07789	307.07915
NH(*n*-Am)	60–62		$C_{12}H_{14}F_3N_3O_4$	321.09353	321.09212
NH(3-Am)	69–71	71–73[e]	$C_{12}H_{14}F_3N_3O_4$		
NH(*n*-Hex)	Oil		$C_{13}H_{16}F_3N_3O_4$	335.10917	335.10827
	92–94		$C_{12}H_8F_3N_3O_4$	331.04152	331.04076
$N(Me)_2$	126–127	124–125[f]	$C_9H_8F_3N_3O_4$		
N(Me)(Et)	112–113		$C_{10}H_{10}F_3N_3O_4$	293.06225	293.06326
$N(Et)_2$	92–94	93–95[f]	$C_{11}H_{12}F_3N_3O_4$		
N(Et)(Pr)	91–92	89–91[f]	$C_{12}H_{14}F_3N_3O_4$		
$N(Pr)_2$	48–49	41–43[f]	$C_{13}H_{16}F_3N_3O_4$		
$N(i\text{-}Pr)_2$	Oil		$C_{13}H_{16}F_3N_3O_4$	335.10917	335.11015
$N(Bu)_2$	39–40	37–39[c]	$C_{15}H_{20}F_3N_3O_4$		
$N(i\text{-}Bu)_2$	71–72	71–72[f]	$C_{15}H_{20}F_3N_3O_4$		
$N(Am)_2$	Oil		$C_{17}H_{24}F_3N_3O_4$	391.17173	391.17269
$N(Hex)_2$	Oil		$C_{19}H_{28}F_3N_3O_4$	419.20301	419.20121
N(Et)(Bu)	67–68	65–67[f]	$C_{13}H_{16}F_3N_3O_4$		
	106–107	100–102[f]	$C_{11}H_{10}F_3N_3O_4$		
	108–109	104–105[f]	$C_{12}H_{12}F_3N_3O_4$		
	64–66		$C_{13}H_{14}F_3N_3O_4$	333.09353	333.09415
	140–141		$C_{11}H_{10}F_3N_3O_5$	321.05716	321.05721
	123–126		$C_{11}H_{11}F_3N_4O_4$	320.07314	320.07266
	88–90		$C_{13}H_{14}F_3N_3O_4$	333.09353	333.09448

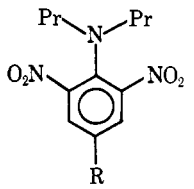
[a] Determined by high-resolution mass spectroscopy. [b] Soper (1963). [c] Malichenko *et al.* (1968). [d] Soper (1967). [e] Soper (1968). [f] Soper (1966).

thesized from 4-di-*n*-propylamino-3,5-dinitrobenzoyl chloride and the appropriate amines by Method L in yields of 40–80%.

4-Methylsulfonyl-2,6-dinitro-*N*,*N*-di-*n*-propylaniline (nitralin) and 3,5-dinitro-*N*,*N*-di-*n*-propylsulfanilamide (oryzalin) were obtained by recrystallization of the technical material from hexane.

Other 4-Substituted Amino-3,5-dinitrobenzotrifluorides. 4-Methylethylamino-3,5-dinitrobenzotrifluoride, 4-diethylamino-3,5-dinitrobenzotrifluoride, 4-ethyl-*n*-propylamino-3,5-dinitrobenzotrifluoride, 4-di-*n*-butylamino-3,5-dinitrobenzotrifluoride, 4-di-iso-butylamino-3,5-dinitrobenzotrifluoride, 4-di-*n*-amylamino-3,5-dinitrobenzotrifluoride, 4-di-*n*-hexylamino-3,5-dinitrobenzotrifluoride, 4-*tert*-butylamino-3,5-dinitrobenzotrifluoride, 4-pyrrolidino-3,5-dinitrobenzotrifluoride, 4-piperidino-3,5-dinitrobenzotrifluoride, 4-(4′-methylpiperidino)-3,5-dinitrobenzotrifluoride, 4-hexamethyleneimino-3,5-dinitrobenzotrifluoride, 4-morpholino-3,5-dinitrobenzotrifluoride, and 4-piperazino-3,5-dinitrobenzotrifluoride were synthesized from 4-chloro-3,5-dinitrobenzotrifluoride and the appropriate amines by Method H. 4-Amino-3,5-dinitrobenzotrifluoride and 4-dimethylamino-3,5-dinitrobenzotrifluoride were synthesized by Method H using concentrated amonium hydroxide and 25% aqueous dimethylamine. 4-Methylamino-3,5-dinitrobenzotrifluoride was synthesized using methylamine hydrochloride and two equivalents of sodium carbonate. These compounds were synthesized in yields of 70–90%.

Table III. Physical Properties of 4-Substituted 2,6-Dinitro-*N*,*N*-di-*n*-propylanilines



R	Melting point, °C		Elemental composition	Molecular weight[a]	
	Observed	Reported		Required	Found
NH_2	84–85		$C_{12}H_{18}N_4O_4$	282.13268	282.13330
OCH_3	42–42.5	Oil[b]	$C_{13}H_{19}N_3O_5$		
Me	41–42	40–42[b]	$C_{13}H_{19}N_3O_4$		
Et	Oil		$C_{14}H_{21}N_3O_4$	295.15322	295.15401
n-Pr	34–36		$C_{15}H_{23}N_3O_4$	309.16883	309.16950
i-Pr	Oil		$C_{15}H_{23}N_3O_4$	309.16883	309.16889
n-Bu	Oil		$C_{16}H_{25}N_3O_4$	323.18435	323.18494
sec-Bu	Oil		$C_{16}H_{25}N_3O_4$	323.18435	323.18557
tert-Bu	53–55		$C_{16}H_{25}N_3O_4$	323.18435	323.18400
H	50–52	50–52[b]	$C_{12}H_{17}N_3O_4$		
F	57–59		$C_{12}H_{16}FN_3O_4$	285.11237	285.11284
Cl	71–72	70–71[b]	$C_{12}H_{16}ClN_3O_4$		
Br	40–41		$C_{12}H_{16}BrN_3O_4$	345.03236	345.03227
COOH	96–100	95–100[b]	$C_{13}H_{17}N_3O_6$		
$CONH_2$	153–155		$C_{13}H_{18}N_4O_5$	310.12759	310.12754
$CON(Me)_2$	119–121	117–119[b]	$C_{15}H_{22}N_4O_5$		
$CON(Et)_2$	86–89		$C_{17}H_{26}N_4O_5$	366.19015	366.18894
$CON(n\text{-}Pr)_2$	Oil		$C_{19}H_{30}N_4O_5$	394.22158	394.22213
$CON(i\text{-}Pr)_2$	Oil		$C_{19}H_{30}N_4O_5$	394.22158	394.22252
Phenyl	81–84		$C_{18}H_{22}N_3O_4$	343.15307	343.15275
p-Nitrophenyl	132–134		$C_{18}H_{21}N_4O_6$	388.17603	388.13939
CN	106–107	104–106[b]	$C_{13}H_{16}N_4O_4$		
CF_3	48–48.5	41–43[b]	$C_{13}H_{16}F_3N_3O_4$		
SO_2CH	148–150	150–151[c]	$C_{13}H_{19}N_3O_6S$		
SO_2NH_3	139–140	137–138[d]	$C_{13}H_{18}N_4O_6S$		
NO_2	138–139	38[e]	$C_{12}H_{16}N_4O_6$	312.10686	312.10661

[a] Determined by high-resolution mass spectroscopy. [b] Soper (1966). [c] Soloway and Zwahlen (1967). [d] Soper (1968). [e] Hollemann (1930).

4-Ethylamino-3,5-dinitrobenzotrifluoride, 4-isopropylamino-3,5-dinitrobenzotrifluoride, 4-*n*-butylamino-3,5-dinitrobenzotrifluoride, 4-isobutyl-3,5-dinitrobenzotrifluoride, 4-*sec*-butyl-3,5-dinitrobenzotrifluoride, 4-*n*-amylamino-3,5-dinitrobenzotrifluoride, 4-*n*-hexylamino-3,5-dinitrobenzotrifluoride, and 4-furfurylamino-3,5-dinitrobenzotrifluoride were synthesized from 4-chloro-3,5-dinitrobenzotrifluoride and the appropriate amines by Method K in yields of 70–90%.

The required amines, with the exception of methylethylamine and ethylpropylamine, were obtained from Aldrich Chemical Co. Ethylpropylamine was obtained from K&K Chemical Co. and methylethylamine was synthesized as below.

Methylethylamine. To 500 g (4.7 mol) of freshly distilled *N*-methylaniline was added dropwise 370 g (2.35 mol) of ethyl iodide, and the mixture slowly warmed to 60°C for 30 min. It was then cooled to room temperature, 200 ml of hexane added, washed several times with 10% sodium carbonate, and the organic phase distilled. The methylethylaniline fraction distilling at 201–203°C (Claus, 1884; 201°C) was collected and redistilled.

To 160 g (1.2 mol) of *N*-methyl-*N*-ethylaniline dissolved in 400 ml of 20% hydrochloric acid was added 91 g (1.3 mol) of sodium nitrite, in small portions, with stirring at 5–10°C. The reaction mixture was then partially neutralized with sodium carbonate and filtered. The crude 4-nitroso-*N*-methyl-*N*-ethylaniline was purified by recrystallization with ethyl alcohol. The yield of product (brilliant green feathers), melting at 69–71°C (Hodgson and Nicholson, 1941; 69°C), was 37% (72 g).

A mixture of 60 g of 4-nitroso-*N*-methyl-*N*-ethylaniline and 500 ml of 25% sodium hydroxide in a 2-l. round-bottomed flask, fitted with a short reflux condenser, and equipped for distillation using a Friedrich condenser cooled to 5°C and capped with a 100-ml round-bottomed flask cooled in a Dry Ice–acetone bath, was heated on a steam cone for 2 hr. Eleven grams (50%) of methylethylamine (bp 36–37°C; Brill, 1932) was collected at the Friedrich condenser.

RESULTS AND DISCUSSION

Two different procedures, "direct" and "indirect," are available for the synthesis of the required 4-alkyl-2,6-dinitrochlorobenzenes. The "direct" route involves the nitration of 4-alkylchlorobenzenes to yield a mixture of mono- and dinitro isomeric products from which the desired product may be isolated with considerable difficulty (Boedtker, 1906). The practical problems associated with the available "indirect" methods varied. Borrows *et al.* (1949) obtained 4-chloro-3,5-dinitrotoluene by treating 2,6-dinitro-4-methylphenol with phosphorus oxychloride in *N*,*N*-diethylaniline; the yield, however, was low (20%). Higher yields could be obtained in the conversion of alkyl dinitrophenols to alkyl dinitrochlorobenzenes, but elaborate procedures were required (Borsche and Feske, 1927; Bunnett *et al.*, 1954; Hawthorne and Cram, 1952). Furthermore, when some of these procedures were applied to the synthesis of 4-alkyl-2,6-dinitrochlorobenzenes, the desired product was not easily isolated from the oily reaction mixture.

The required 4-substituted 2,6-dinitrochlorobenzenes (with the exception of picryl chloride) which contain a meta-direct-

ing substituent (*e.g.*, COOH, CF_3) are readily obtained by either the nitration of a 4-substituted chlorobenzene or the nitration of a 4-substituted phenol and subsequent chlorodehydroxylation. 4-Substituted 2,6-dinitrochlorobenzenes containing an ortho–para directing substituent (*e.g.*, Cl, CH_3) are readily obtained *via* the nitration of a 4-substituted phenol and chlorodehydroxylation.

It was found that mixtures of phosphorus oxychloride and DMF are general for the conversion of dinitrophenols to corresponding dinitrochlorobenzenes. The addition of DMF greatly enhances the chlorinating properties of phosphorus oxychloride. For example, picric acid is unreactive to phosphorus oxychloride (Boyer *et al.*, 1946), but is readily converted to picryl chloride by phosphorus oxychloride containing small amounts of DMF. The amount of DMF required and the ease of chlorodehydroxylation of 4-substituted 2,6-dinitrophenols are dependent upon the electronic properties of the 4-substituent (Table I). Picric acid is readily chlorinated by phosphorus oxychloride containing catalytic quantities of DMF in approximately 20 min. However, a large excess of DMF and a reaction time of 16 hr are required for the chlorination of 4-alkyl-2,6-dinitrophenols.

All of the dinitroanilines, except 4-amino-3,5-dinitro-*N*,*N*-di-*n*-propylaniline and 4-di-isopropylamino-3,5-dinitrobenzotrifluoride, are readily prepared by the aminodechlorination of the appropriate 4-substituted 2,6-dinitrochlorobenzenes. The conversion of 4-amino-2,6-dinitrochlorobenzene to 4-amino-2,6-dinitro-*N*,*N*-di-*n*-propylaniline was attempted by Method J; however, no product was obtained due to the inactivating amino group (Miller and Williams, 1953). This conversion was also attempted *via* the N-acetyl derivative, but the desired product was obtained in a very poor yield and was extremely difficult to isolate from the conglomeration of unidentified reaction products. 4-Amino-2,6-dinitro-*N*,*N*-di-*n*-propylaniline is easily obtained, however, *via* the decomposition of the corresponding 4-carboxyazido-2,6-dinitro-*N*,*N*-di-*n*-propylaniline. The conversion of 4-chloro-3,5-dinitrobenzotrifluoride to 4-di-isopropylamino-3,5-dinitrobenzotrifluoride was only achieved under forcing conditions and in poor yield (5–7%). Attempts to increase the yield by using higher temperatures than in Method J or stronger reagents such as sodium di-isopropylamide were ineffective and resulted in lower yields.

The physical properties of 4-substituted 3,5-dinitrobenzotrifluorides and 4-substituted 2,6-dinitro-*N*,*N*-di-*n*-propylanilines are presented in Tables II and III. The elemental composition (high-resolution mass spectroscopy) and nmr spectra (not reported) are consistent with the proposed structures.

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