589. *The Separation of Aromatic Amines by Partition Chromatography. Part I. An Investigation of the* N-*Alkylation of* 3 : 5-*Dinitroaniline.*

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Five *N*-alkyl and two *NN*-dialkyl derivatives of 3 : 5-dinitroaniline have been prepared by various methods; an efficient procedure for their separation and purification by partition chromatography is described.

In an attempt to prepare 3 : 5-dinitrophenyltrimethylammonium bromide, 3 : 5-*dinitroaniline hydrobromide* was heated with methanol for 48 hours at 100° in a sealed tube. By analogy with the reaction of *m*-nitroaniline hydrobromide with methanol (Schliom, *J. pr. Chem.*, 1902, [ii], **65**, 252—257) it was expected that the quaternary ammonium salt would be obtained, whereas, in fact, 3 : 5-*dinitrodimethylaniline* was isolated as the only product and in 65% yield. All attempts to convert this compound into a quaternary ammonium salt were unsuccessful.

A more complete examination of the *N*-alkylation of the primary amine was then carried out. The only recorded work on this problem appeared to be that of Blanksma (*Rec. Trav. chim.*, 1902, **21**, 266) who claimed the production of 3 : 5-dinitromethyl- and 3 : 5-dinitrodimethyl-aniline by interaction of the primary amine (1 mol.) with a methanolic solution of methyl iodide (1 mol.) in a sealed tube for 3 hours at 100°, but did not record any analytical data or separation of the products.

N-Alkylation was attempted by (*a*) prolonged heating of 3 : 5-dinitroaniline hydrobromide with the appropriate alcohol in a sealed tube, (*b*) treatment of 3 : 5-*dinitroformanilide* with an alkyl halide and subsequent hydrolysis to the secondary amine, and (*c*) treatment of the primary amine with an alkyl sulphate. An attempt to prepare 3 : 5-dinitrodiethylaniline from bromo-3 : 5-dinitrobenzene by treatment with diethylamine failed (cf. Holleman and ter Weel, *Rec. Trav. chim.*, 1915, **35**, 48).

During our work it became apparent that increasing the chain length of the alkylating group always increased the difficulty of *N*-alkylation, this effect being most marked when passing from methyl to ethyl. 3 : 5-*Dinitro*-N-*methylaniline* was obtainable only by method (*a*) when a mixture of the primary base with its hydrobromide was used; even so, a considerable proportion of the tertiary amine was also produced. Reaction of 3 : 5-dinitroaniline hydrobromide with ethanol under the conditions used in the preparation of 3 : 5-dinitrodimethylaniline yielded 3 : 5-*dinitroethylaniline* as the only product and in high yield (80%). 3 : 5-*Dinitro*-n-*propyl*-, 3 : 5-*dinitro*-n-*butyl*-, and 3 : 5-*dinitro*-n-*amyl-aniline* were similarly obtained, but in decreasing yields.

Direct dialkylation of the amino-group of 3 : 5-dinitroaniline was successful only in the preparation of 3 : 5-dinitrodimethylaniline. 3 : 5-*Dinitrodiethylaniline* was obtained by prolonged reaction of 3 : 5-dinitroethylaniline with an excess of ethyl iodide at 100°, a considerable quantity of the secondary amine remaining unchanged. A similar reaction between 3 : 5-dinitro-*n*-propylaniline and *n*-propyl iodide yielded insufficient tertiary amine for characterisation.

The *N*-alkyl and *NN*-dialkyl derivatives are highly coloured, the secondary amines being in general yellow and the tertiary amines orange. They are apparently very weak bases; they dissolve quite readily in concentrated hydrochloric acid but the addition of even a small quantity of water to the solution precipitates the free amines.

Some difficulty was at first encountered in separating and purifying the mixtures of primary, secondary, and tertiary bases which were frequently obtained. Fractional crystallisation proved ineffective, yielding, in some cases, an apparently pure crystalline compound which was shown by analysis to be a complex containing equimolecular quantities of, for example, primary and secondary bases. It is well known that the Hinsberg method of separating mixed amines (*Ber.*, 1905, **38**, 906) is often inapplicable to nitrated phenylamines. We found that 3 : 5-dinitroaniline would not react with toluene-*p*-sulphonyl chloride when the usual techniques were employed. Further, in test experiments with 3 : 5-dinitroaniline and 3 : 5-dinitroethylaniline, the technique developed by Alexander and McElvain (*J. Amer. Chem. Soc.*, 1938, **60**, 2286) failed; first because the high temperature (210°) necessary to convert the 3-nitrophthalamic acid, derived from the primary base, into the corresponding imide caused decomposition of some of the reactants, and secondly because 3-nitrophthalic anhydride did not react quantitatively with the secondary amine.

Amines may be separated by taking advantage of their different basic strengths, in a process

involving partition of the bases between an aqueous acid layer and an immiscible solvent. We have increased the efficiency of this process, using the principles of partition chromatography (Martin and Synge, *Biochem. J.*, 1941, **35**, 1358; Gordon, Martin, and Synge, *ibid.*, 1943, **37**, 79). The use of a buffered immobile phase has been shown to have certain advantages (Craig, Golumbic, Mighton, and Titus, *J. Biol. Chem.*, 1945, **161**, 321; Fischbach, Eble, and Mundell, *J. Amer. Pharm. Assoc.*, 1947, **36**, 220). Since the bases with which we were concerned were appreciably soluble only in fairly concentrated mineral acids, it was obvious that a strongly acid immobile phase was required. Eventually a most efficient separation of mixtures of the primary, secondary, and tertiary bases was obtained by use of hydrochloric or sulphuric acid (6—25N.), absorbed in " Supercel " kieselguhr, as the immobile phase, and pure chloroform, saturated with the appropriate acid solution, as the mobile phase. Clear separations, with almost quantitative recoveries, were then possible.

Some difficulty was encountered in the persistence of silica, presumably in colloidal form, in the products obtained after separation on kieselguhr. This inorganic material, together with the water which it retained, caused incorrect analytical figures. This contaminant was eventually removed by filtration of a solution of the amine in concentrated hydrochloric acid through a sintered-glass filter of fine pore-size.

We think it highly probable that this method will be applicable to mixtures of other amines and particularly to mixtures of other nitrated amines, since these generally possess sufficient colour greatly to facilitate chromatographic separation.

Experimental.

Chromatographic Procedure.—The standard technique of partition chromatography was followed except that, in place of buffer solutions, mineral acids of strengths ranging from 6N to 25N were employed in the immobile phase. The appropriate acid solution was intimately mixed with purified " Supercel " kieselguhr to form a gel containing 40—50% (w/w) of the acid solution. A Pyrex tube *ca.* 40 cm. long and 2·5 cm. in diameter was filled with pure chloroform, previously equilibrated with the appropriate acid solution, and *ca.* 90 g. of the gel were added in small quantities under slight suction (*ca.* 10 mm. of mercury). Each portion of the gel was agitated to remove air bubbles and was then pressed down with a glass plunger. The upper surface was protected with a thin layer of glass wool, and the whole column was then washed with 200 ml. of acid-saturated chloroform. Columns containing 50% (w/w) of 6N- and 8N-hydrochloric acid and 40% (w/w) of 15N-, 20N-, and 25N-sulphuric acid were prepared in this manner.

The solution under examination, containing not more than 300 mg. of material, was delivered on to the surface of the appropriate gel, and the chromatogram developed with pure, acid-saturated chloroform under positive pressure. A suitable arrangement of taps allowed the solvent reservoir to be renewed without releasing the pressure at the top of the column. 5-Ml. fractions were collected from the base of the column. Successive " cuts " containing the separated amines were combined, the chloroform was evaporated, and the residue dissolved in concentrated hydrochloric acid. The solution was boiled for 30 seconds and filtered through a sintered-glass filter of maximum pore size 1·4 μ. The filtrate was cooled and made alkaline, and the amine extracted with ether. Crystallisation from aqueous alcohol yielded the pure amine.

Model Experiment on the Separation of Primary, Secondary, and Tertiary Bases.—Preliminary experiments showed that 3 : 5-dinitromethyl- and 3 : 5-dinitrodimethyl-aniline were not separable on a column containing 6N-hydrochloric acid, but that the primary base ran too slowly on a column containing 8N-hydrochloric acid. The following procedure appeared the most efficient.

3 : 5-Dinitroaniline (100 mg.; m. p. 160°), 3 : 5-dinitromethylaniline (90 mg.; m. p. 158°), and 3 : 5-dinitrodimethylaniline (100 mg.; m. p. 164°) were dissolved in chloroform, and the solution was loaded on to a column of length 17 cm. and diameter 2·5 cm., containing 6N-hydrochloric acid. Development was carried out using acid-saturated chloroform under a positive pressure of 10 mm. of mercury, the flow rate being 7·1 c.c. per minute. Separation into two bands rapidly occurred and 5-ml. cuts were collected. The concentration per cut was measured by means of a " Spekker " photoelectric absorptiometer, calibration curves having previously been plotted for 3 : 5-dinitroaniline (Ilford Spectrum Violet filter, No. 601) and for 3 : 5-dinitromethyl- and 3 : 5-dinitrodimethyl-aniline (Ilford Spectrum Blue/Green filter, No. 603). The results are shown graphically in Fig. 1. Cuts 45—70 yielded 90 mg. of the primary base (identified by m. p. and mixed m. p. with an authentic sample). Cuts 9—29, containing the secondary and tertiary amines, were concentrated to small bulk and loaded on to a column of length 39 cm. and diameter 2·5 cm., containing 8N-hydrochloric acid. Under a positive pressure of 50 mm. of mercury the flow rate was 7·1 c.c. per minute. 5-Ml. cuts were taken. The separation is shown in Fig. 2. Cuts 10—19 yielded 95 mg. of the tertiary base (m. p. 164°) and cuts 50—80 yielded 85 mg. of the secondary base (m. p. 157—158°). Neither of these samples depressed the m. p. of an authentic specimen.

3 : 5-*Dinitroaniline.*—*s*-Trinitrotoluene was oxidised to *s*-trinitrobenzoic acid. The acid was decarboxylated to *s*-trinitrobenzene (*Org. Synth.*, Vol. II, 93), one nitro-group of which was preferentially reduced (Flürscheim, *J. pr. Chem.*, 1905, [ii], **71**, 537), yielding 3 : 5-dinitroaniline (m. p. 160—161°; yield, 40%). The method was modified slightly in that the crude amine was obtained by pouring the reaction product into three times its volume of ice-water, thus considerably reducing the amount of resinification caused by the prolonged heating prescribed in the original method. Some 1-nitro-3 : 5-diaminobenzene was also isolated.

3 : 5-*Dinitroaniline hydrobromide*.—3 : 5-Dinitroaniline (1 mol.) and constant-boiling hydrobromic acid (1·1 mols.) were kept in a corked vessel for 2 days; the product was then pressed dry under suction. 3: 5-*Dinitroaniline hydrobromide* was obtained (yield, almost 100%) as a grey amorphous powder of indeterminate m. p. (Found : Br, 31·0. $C_6H_5O_4N_3$,HBr requires Br, 30·3%).

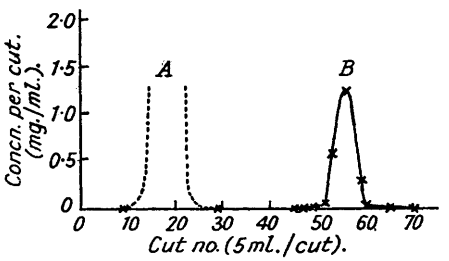
Synthesis of the Secondary Amines.—The following general method was adopted. 3 : 5-Dinitroaniline hydrobromide (1 g., 1 mol.) was heated with the appropriate alcohol (6 mols.) in a sealed tube at 100° for 48 hours. The excess of alcohol was removed under reduced pressure. The product was freed from tarry matter by crystallisation from aqueous alcohol (charcoal) and was then always obtained as a mixture of the free bases. By this technique the following secondary amines were obtained.

(*a*) 3 : 5-*Dinitroethylaniline* formed brilliant orange needles, m. p. 185—186° (56% yield) (Found : C, 45·6; H, 4·2; N, 19·7. $C_8H_9O_4N_3$ requires C, 45·5; H, 4·3; N, 19·9%). The product from a second experiment was purified chromatographically on a column containing 6N-hydrochloric acid, and the base was obtained in 72% yield from cuts 8—22, the unchanged 3 : 5-dinitroaniline being recovered from cuts 35—55. Further examination of the alkylated fraction on a column containing 8N-acid showed the product to be homogeneous.

(*b*) 3 : 5-*Dinitro*-n-*propylaniline* crystallised in yellow plates, m. p. 129—130°, in poor yield (Found : C, 48·1; H, 4·8; N, 18·8. $C_9H_{11}O_4N_3$ requires C, 47·9; H, 4·9; N, 18·7%). A considerable quantity of tarry matter was produced but, in a second experiment, the yield was improved to 29% by chromatographic purification, the secondary amine being obtained from cuts 6—15 and the unchanged primary amine from cuts 41—70 from a column containing 6N-hydrochloric acid. Further analysis of the alkylated fraction on a column containing 8N-acid effected no resolution.

FIG. 1.

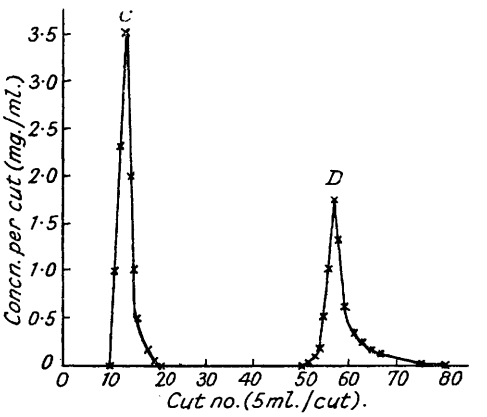
Separation of amines by partition chromatography (amounts recovered are given in parentheses).



Immobile phase : 6N-*hydrochloric acid. A = a mixture* (190 *mg.*) *of* 3 : 5-*dinitromethylaniline and* 3 : 5-*dinitrodimethylaniline. B =* 3 : 5-*dinitroaniline* (90 *mg.*).

FIG. 2.

Separation of amines by partition chromatography (amounts recovered are given in parentheses).



Immobile phase : 8N-*hydrochloric acid. C =* 3 : 5-*dinitrodimethylaniline* (95 *mg.*). *D =* 3 : 5-*dinitromethylaniline* (85 *mg.*).

(*c*) 3 : 5-*Dinitro*-n-*butylaniline* was obtained as yellow plates, m. p. 99° (about 17% yield) (Found : C, 50·6; H, 5·4; N, 17·5. $C_{10}H_{13}O_4N_3$ requires C, 50·2; H, 5·5; N, 17·6%), chromatography being necessary for purification of the product. The supposed secondary amine was obtained, on a column containing 6N-hydrochloric acid, from cuts 8—18 and the unchanged primary base from cuts 33—57. Further examination of the alkylated fraction on an 8N-hydrochloric acid column gave only one band (cuts 16—26) but when the run was repeated on a column containing 15N-sulphuric acid an indication of separation into two bands was observed. On a column containing 20N-sulphuric acid a clear separation occurred, the 3 : 5-dinitro-*n*-butylaniline being obtained from cuts 38—77 and a small quantity of an orange substance, presumably 3 : 5-dinitrodi-*n*-butylaniline from its position relative to the secondary base, from cuts 17—27.

(*d*) 3 : 5-*Dinitro*-n-*amylaniline*. Chromatographic purification was employed, the unchanged primary amine being recovered from cuts 30—50 and the alkylated amine from cuts 6—20 from a column containing 6N-hydrochloric acid. The alkylated material was then chromatographed on a column containing 20N-sulphuric acid, one band only being obtained (from cuts 16—40). A further run on a column containing 25N-sulphuric acid, however, produced two definite bands, one from cuts 31—44 which yielded a very small quantity of, presumably, tertiary amine and a second which first appeared in cut 79 and which divided into two subsidiary bands as elution proceeded. The first of these, from cuts 79—135, gave the required 3 : 5-*dinitro*-n-*amylaniline* as yellow plates, m. p. 88—90°, in 5% yield (Found : C, 52·5; H, 5·5; N, 16·5. $C_{11}H_{15}O_4N_3$ requires C, 52·2; H, 5·9; N, 16·6%). Reaction with nitrous acid yielded a nitrosoamine (positive Liebermann reaction). The material in the second band was recovered by extruding the gel and, after purification, yielded yellow crystals, m. p. 88°, which, although showing the characteristic reactions of a secondary amine, were not identical with the previously described 3 : 5-dinitro-*n*-amylaniline (mixed m. p. 72°), were not identifiable on analysis, and were not further investigated.

Attempted Preparation of 3 : 5-*Dinitro*-n-*hexylaniline*.—*n*-Hexyl alcohol (6 mols.) was heated with

3 : 5-dinitroaniline hydrobromide for 48 hours in a sealed tube at 100°. The product was freed from primary base (cuts 26—46), the alkylated amine being obtained from cuts 7—14 on a column containing 6N-hydrochloric acid. This material was then chromatographed on columns containing 20N- and 25N-sulphuric acid, but no separation was achieved. The use of 30N-sulphuric acid in the immobile phase caused considerable decomposition. Analysis of the product from the 25N-column showed that it still contained a small proportion of tertiary amine.

3 : 5-*Dinitromethylaniline*.—Formic acid was dried by the method of Pyranishnikov and Shakovah (*J. Gen. Chem. Russia*, 1932, **2**, 821; *Chem. Abs.*, 1933, **27**, 2672) and determined volumetrically as 99·5% pure. The acid (8 mols.) was heated under reflux under strictly anhydrous conditions with 3 : 5-dinitroaniline (1 mol.) for 12 hours. The reaction product was poured into ice-water. The 3 : 5-*dinitroformanilide* (50%) crystallised from ligroin (b. p. 80—100°) as colourless aggregates of stout rods, m. p. 119° (Found : C, 40·0; H, 2·4; N, 19·7. $C_7H_5O_5N_3$ requires C, 39·8; H, 2·4; N, 19·9%). The alkylation was carried out by heating the formanilide (1 mol.) with methyl iodide (1·3 mols.) in the minimum of absolute methanol under reflux and adding dropwise, during 15 minutes, a solution of potassium hydroxide (1·3 mols.) in absolute methanol, under strictly anhydrous conditions (King and Tonkin, *J.*, 1946, 1068; cf. Pictet and Crépieux, *Ber.*, 1888, **21**, 1106). The solid material was isolated by pouring the product into ice-water, and hydrolysis to 3 : 5-*dinitromethylaniline* was completed by boiling the solid with the minimum of 48% hydrobromic acid. The 3 : 5-dinitromethylaniline, obtained by pouring the mixture into ice-water, appeared, after four recrystallisations from aqueous alcohol (charcoal), as orange-yellow needles, m. p. 158° (Found : C, 42·9; H, 3·4; N, 21·0. $C_7H_7O_4N_3$ requires C, 42·7; H, 3·6; N, 21·3%). The yield was 17%, based on 3·5-dinitroaniline.

This secondary amine was also prepared by alkylating a mixture of 3 : 5-dinitroaniline (0·6 mol.) and 3 : 5-dinitroaniline hydrobromide (0·4 mol.) with methanol (6 mols.) in a sealed tube at 100° for 48 hours. There was obtained a mixture (m. p. 123°) of 3 : 5-dinitromethyl- and 3 : 5-dinitrodimethylaniline, which was separated chromatographically. A preliminary run on a column containing 6N-hydrochloric acid showed the absence of primary base, one band only being obtained (cuts 8—20). Subsequent analysis of this fraction on an 8N-column yielded 3 : 5-dinitrodimethylaniline (m. p. 164°) from cuts 24—34 and 3 : 5-dinitromethylaniline (m. p. 158°; 55%) from cuts 52—86.

3 : 5-*Dinitroethylaniline*.—In addition to the general method already described, the synthesis of this secondary amine was also attempted by ethylation of the formanilide. The technique used was as for the methyl analogue, but only a partly alkylated product was isolated. This product, on repeated recrystallisation from aqueous alcohol (charcoal) and from ligroin (b. p. 100—120°), melted at 139° and appeared to be a complex containing equimolecular proportions of 3 : 5-dinitroaniline and 3 : 5-dinitroethylaniline (Found : C, 42·2; H, 3·25; N, 21·4. Calc. for $C_8H_9O_4N_3,C_6H_5O_4N_3$: C, 42·4; H, 3·5; N, 21·4%). An attempt to achieve alkylation by the same technique, but with use of dry xylene as solvent, gave the same results. Resolution on a column containing 6N-hydrochloric acid yielded 3 : 5-dinitro-*N*-ethylaniline (m. p. 184—185°) from cuts 9—17, and 3 : 5-dinitroaniline (m. p. 159°), from cuts 33—55, in equal amounts.

3 : 5-*Dinitrodimethylaniline*.—3 : 5-Dinitroaniline hydrobromide (1 mol.) was treated with methanol (6 mols.) in a sealed tube at 100° for 48 hours. The excess of methanol was removed *in vacuo*. 3 : 5-*Dinitrodimethylaniline* (65%) was obtained on recrystallisation from aqueous alcohol (charcoal) as orange needles, m. p. 164° (Found : C, 45·5; H, 4·3; N, 19·9. $C_8H_9O_4N_3$ requires C, 45·5; H, 4·3; N, 19·9%).

3 : 5-*Dinitrodiethylaniline*.—(*a*) 3 : 5-Dinitroaniline hydrobromide (0·5 g., 1 mol.) was heated with a large excess of anhydrous ethanol (1·33 ml., 12 mols.) at 190° for 9 hours in a sealed tube with potassium iodide (0·04 g.), cuprous chloride (0·015 g.), and calcium chloride (0·025 g.) as catalyst (Johnson, Hill, and Donleavy, *Ind. Eng. Chem.*, 1920, **12**, 636). Considerable decomposition occurred at this temperature, and the experiment was repeated at 150—160°. In neither case was any tertiary amine isolated.

(*b*) 3 : 5-Dinitroaniline (1 g., 1 mol.) and calcium hydroxide (0·49 g.) were dissolved in the minimum of dry xylene at 80°, and redistilled ethyl sulphate (3·0 ml., 3 mols.) was added. The temperature was raised to 145°. After 2 hours some decomposition appeared to be taking place and the temperature was maintained at 120° for a further 2 hours. Although Cade (*Chem. Met. Eng.*, 1923, **29**, 319) claims 90% yields of diethylaniline by this method, the only product isolated in our experiment was 3 : 5-dinitroethylaniline, m. p. 185°.

(*c*) 1-Bromo-3 : 5-dinitrobenzene, m. p. 75° (Bader, *Ber.*, 1891, **24**, 1653), when treated for 24 hours at 100° with diethylamine (12 mols.), was recovered unchanged (cf. Holleman and ter Weel, *loc. cit.*).

(*d*) 3 : 5-Dinitroethylaniline (0·5 g., 1 mol.), purified chromatographically as already described, was heated, for 100 hours in a sealed tube at 100°, with ethyl iodide (1·5 ml., 11 mols.) and an equal volume of ethanol (to act as solvent and to absorb any hydrogen iodide formed). The product was extracted in the usual manner. 300 Mg. were dissolved in chloroform and separated on a column containing 8N-hydrochloric acid. 3 : 5-*Dinitrodiethylaniline* (150 mg.), m. p. 112° (26·5%) (Found : C, 50·0; H, 5·0; N, 17·4. $C_{10}H_{13}O_4N_3$ requires C, 50·2; H, 5·5; N, 17·5%), was obtained from cuts 31—44, and unchanged 3 : 5-dinitroethylaniline (150 mg.), m. p. 185°, from cuts 59—76.

Attempted Preparation of 3 : 5-*Dinitrodi-*n*-propylaniline*.—By a procedure similar to (*d*) above, 3 : 5-dinitro-*n*-propylaniline and *n*-propyl iodide yielded a very small quantity (insufficient for characterisation) of an orange material from cuts 18—34 from a column containing 20N-sulphuric acid. Cuts 80—138 yielded unchanged secondary amine.

Attempts to Form a Quaternary Ammonium Salt from 3 : 5-*Dinitrodimethylaniline*.—(*a*) 3 : 5-Dinitrodimethylaniline (1 mol.), when heated at 100° with methyl iodide (2 mols.) in dry methanol for 24 hours, acetonitrile for 8 hours, or nitromethane for 24 hours, gave products containing no ionisable halogen.

(*b*) 3 : 5-Dinitrodimethylaniline (1 mol.) was heated with methyl sulphate (1·5 mols.) in dry nitrobenzene at 100—110° for 10 minutes (cf. Kehrmann and Havas, *Ber.*, 1913, **46**, 341). The tertiary amine was recovered unchanged. An attempt to prepare 3 : 5-dinitrophenylmethyldiethylammonium methosulphate by this method also failed.

Reaction of 3 : 5-*Dinitroaniline and* 3 : 5-*Dinitroethylaniline with* 3-*Nitrophthalic Anhydride*.—A solution of 3 : 5-dinitroaniline (0·95 g.) and 3-nitrophthalic anhydride (*Org. Synth.*, Vol. VII, pp. 70, 74)

(1 g.) in benzene (7·5 ml.) was heated under reflux for 30 minutes. Almost colourless crystals (1·7 g.), m. p. 205°, were deposited from the cooled solution. 1·5 G. of this compound were heated at 160° in an oil-bath for 30 minutes. No change occurred (cf. Alexander and McElvain, *loc. cit.*). After the mixture had been heated at 210° for 10 minutes it darkened slightly and the product, after recrystallisation from aqueous alcohol–acetone (charcoal), melted sharply at 225°. This material, 3-*nitro*-N-3′ : 5′-*dinitrophenylphthalimide*, was insoluble in sodium carbonate solution (Found : C, 46·9; H, 1·7; N, 15·5. $C_{14}H_6O_8N_4$ requires C, 47·0; H, 1·7; N, 15·6%). An attempt to regenerate the primary base by heating this product under reflux first with 10% sodium hydroxide solution (to open the phthalimide ring) and then with 10% hydrochloric acid (to remove the 3-nitrophthaloyl group) led to a large amount of tar; very little 3 : 5-dinitroaniline could be recovered.

3 : 5-Dinitroethylaniline (0·5 g.) and 3-nitrophthalic anhydride (0·5 g.) were heated under reflux in benzene (5 ml.) for 11 hours. The benzene was removed and two distinct crystal types were observed. Extraction with sodium hydrogen carbonate solution left a residue of material, m. p. 183° alone or mixed with 3 : 5-dinitroethylaniline. The remainder of the secondary base (*ca.* 50%) was recovered by heating the soluble portion, presumably containing the 3-nitro-2-(*N*-3′ : 5′-dinitrophenyl-*N*-ethylcarbamyl)-benzoic acid, with 10% hydrochloric acid under reflux for 30 minutes and subsequently rendering the solution alkaline. A possible separation, involving the above reactions, was thus shown to compare so unfavourably with the chromatographic procedure already described that it was abandoned.

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