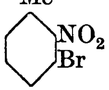
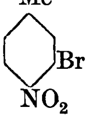
CCCLXV.—*Monohalogenomononitrotoluenes. Arsenical Compounds derived from 3-Bromo-4-nitrotoluene.*

By Leslie Alderman Elson, Charles Stanley Gibson, and John Dobney Andrew Johnson.

When the synthesis of various nitrodiphenylamine-6′-arsinic acids was commenced and their reduction products and the production of derivatives of 10-chloro-5 : 10-dihydrophenarsazine were studied (Gibson and Johnson, this vol., p. 1229), only seven of the ten theoretically possible monobromonitrotoluenes were known. An eighth, *viz.*, 2-bromo-3-nitrotoluene, was described in the above-mentioned paper (p. 1243) and the two remaining ones, *viz.*, 3-*bromo*-2-*nitrotoluene* (I) and 3-*bromo*-4-*nitrotoluene* (II), are now described. The latter substance has been prepared by direct synthesis, and the former by what appears to be a unique reaction.

(I.)



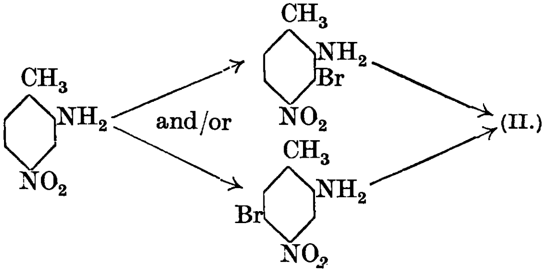


(II.)

The chlorine analogue of (II) was shown by Reverdin and Crépieux (*Ber.*, 1900, **33**, 2505) to be formed, together with 5-chloro-2-nitrotoluene, by nitration of *m*-chlorotoluene; but the substance has been isolated only by Wibaut (*Rec. trav. chim.*, 1913, **32**, 244), who chlorinated aceto-*o*-toluidide, nitrated the product, and removed the acetamido-group. Wroblewski (*Annalen*, 1873, **168**, 170) and

Grete (*ibid.*, 1875, **177**, 246) nitrated *m*-bromotoluene, and the crystalline substance they isolated has been shown to be 5-bromo-2-nitrotoluene (Gibson and Johnson, *loc. cit.*, p. 1245).

An attempt was first made to introduce a bromine atom into the nucleus of 4-nitro-2-aminotoluene; the two most probable products should both yield 3-bromo-4-nitrotoluene on deamination.



Unfortunately, a dibromo-derivative was produced, as Morgan and Clayton (J., 1905, **87**, 951) have shown.

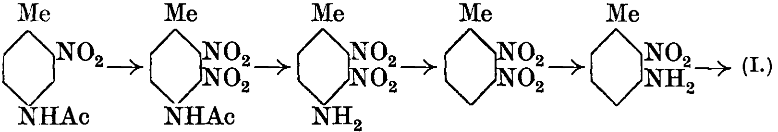
The next line of attack was to try to prepare 4-nitro-3-aminotoluene, from which the required bromonitrotoluene (II) should be accessible by means of the Sandmeyer reaction. The methods of Brady and Cook (J., 1920, **117**, 752; compare Cohen and Dakin, J., 1903, **83**, 333) and of Städel and Kolb (*Annalen*, 1890, **259**, 224) were found to be unsuitable for the preparation of this nitroamine in quantity. We also attempted to prepare it from 5-nitro-2-aminotoluene by the methods of Morgan and Micklethwait (J., 1913, **103**, 1399) and of Morgan and Scharff (J., 1914, **105**, 121): *5-amino-2-acetamidotoluene* was obtained by the reduction of 5-nitro-2-acetamidotoluene and from it we prepared 4-nitro-2 : 5-diaminotoluene as described by these authors, but the partial deamination of this nitrodiamine to 4-nitro-3-aminotoluene by us was nothing like so successful as by Morgan and his co-workers, who obtained a yield of 60—70%. We finally prepared 4-nitro-3-aminotoluene in good yield by the action of methyl-alcoholic ammonia on 3 : 4-dinitrotoluene (Page and Heasman, J., 1923, **123**, 3235) according to the method of Kenner and Parkin (J., 1920, **117**, 858).

From the nitroamine, 3-chloro-, 3-bromo-, and 3-iodo-4-nitrotoluenes were prepared by means of the Sandmeyer reaction. The first two compounds are amongst the lowest-melting of their isomerides, but *3-iodo-4-nitrotoluene* is one of the highest-melting of its isomerides. Previous to this work, nine of the ten theoretically possible iodonitrotoluenes had been rationally synthesised; Beilstein and Kuhlberg (*Annalen*, 1871, **158**, 350), by nitration of *m*-iodotoluene, obtained what should, by elimination, be the tenth isomeride—3-iodo-4-nitrotoluene. The properties of the substance they describe agree very closely with those of the pure substance now rationally synthesised.

One anomaly concerning the iodonitrotoluenes occurs in the literature, *viz.*, that on nitration of *o*-iodotoluene, 2-iodo-4-nitrotoluene, m. p. 102°, is produced (Datta and Varma, *J. Amer. Chem. Soc.*, 1919, **41**, 2047). This substance has, however, been rationally synthesised by many workers and has a much lower melting point (58°). The product obtained by Datta and Varma would appear to be 2-iodo-5-nitrotoluene (m. p. 103—104°), which has been prepared by Reverdin and Kăcer (*Ber.*, 1897, **30**, 3000) from the corresponding nitroamine.

Two references to 3-bromo-2-nitrotoluene occur in the literature. Nevile and Winther (*Ber.*, 1880, **13**, 1945) stated that by nitration of 3-bromo-5-acetotoluidide, followed by hydrolysis and deamination, 3-bromo-2-nitrotoluene was obtained as an uncrystallisable oil, volatile in steam. The nitro-group was oriented in the conventional manner. The scanty details recorded by these authors make it impossible to repeat their work, but it is clear that the supposed 3-bromo-2-nitrotoluene was impure, since the pure substance is a solid, m. p. 27°. Burton and Kenner (J., 1926, 1802) mercurated *o*-nitrotoluene and oriented the products by treatment with bromine in potassium bromide solution. 4-Bromo-2-nitrotoluene was isolated in the pure state in small yield, and the presence of 3-bromo-2-nitrotoluene in the major oily portion of the product was demonstrated by oxidation to the corresponding bromonitrobenzoic acid. 3-Bromo-2-nitrotoluene was, however, not isolated.

The synthesis of 3-bromo-2-nitrotoluene was attempted by means of the following series of reactions :



(III.) (IV.)

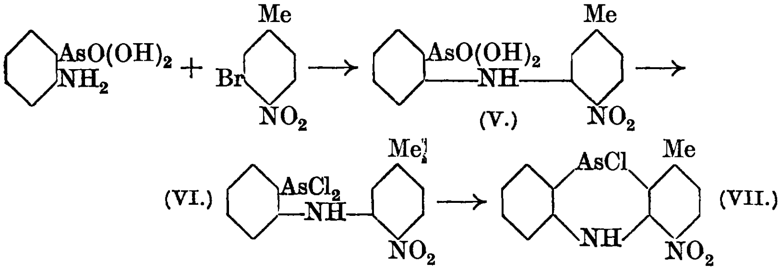
The first three stages have been described by Page and Heasman (*loc. cit.*, p. 3239) and the fourth by Kenner and Parkin (J., 1920, **117**, 855) and by Burton and Kenner (J., 1921, **119**, 1051). Substance (III) was readily obtained, but, as the details recorded for its conversion into (IV) proved to be inadequate, an alternative method of deamination was attempted. The dinitrotoluidine, mixed with concentrated hydrochloric acid and alcohol and treated with a solution of sodium nitrite, furnished a moderate yield of a chloronitrotoluene, m. p. 21—22°. The four chloronitrotoluenes most likely to be formed from (III) are (*a*) 3-chloro-2-nitrotoluene, (*b*) 4-chloro-2-nitrotoluene, (*c*) 2-chloro-3-nitrotoluene, and (*d*) 4-chloro-3-nitrotoluene, (*a*) and (*c*) being the most probable. The substance was shown not to be (*c*) and appeared to be (*a*), since the melting point given for (*a*) is 21—22°. Substance (*a*) is the chlorine analogue of the required bromonitrotoluene and the deamination of (III) was therefore carried out with 36% hydrobromic acid instead of hydrochloric acid; a 45% yield of 3-bromo-2-nitrotoluene was obtained. It was shown to be different from seven isomerides (marked with an asterisk in the following table) and the final proof of its constitution was furnished by the bromonitrobenzoic acid (m. p. 249—253°) which it yielded on oxidation.

An attempt was made to extend this interesting reaction, in which an amino-group is replaced by a hydrogen atom and at the same time a nitro-group is replaced by a bromine atom, to other dinitrotoluidines. 2 : 6-Dinitro-*p*-toluidine gave no bromonitrotoluene. It appeared probable that the peculiar reactivity of the 3-nitro-group in (III) had its origin in the vicinal character of the various groups. We therefore attempted to prepare 3-bromo-4-nitrotoluene from 3 : 4- and 4 : 5-dinitro-*o*-toluidines, but only from the former were we able to isolate a small quantity of it.

The most probable melting points of the halogenonitrotoluenes are given in the following table :

CH_3 : NO_2 : X.	X = Cl.	X = Br.	X = I.
1 : 2 : 3	23·4°	27°	65°
1 : 2 : 4	38	*46	61
1 : 2 : 5	24·9	*55	84
1 : 2 : 6	35·3	*41	35·5
1 : 3 : 2	22·1	*42	68
1 : 3 : 4	7	*33	55
1 : 3 : 5	58·4	82	77
1 : 3 : 6	42·9	*78	104
1 : 4 : 2	62·3	*78	58
1 : 4 : 3	24·2	37	105

The condensation of 3-bromo-2-nitrotoluene (I) with *o*-aminophenylarsinic acid under the conditions previously described (this vol., p. 1246) did not yield a satisfactory product, but from 3-bromo-



(V.)

(VI.)

(VII.)

4-nitrotoluene and *o*-aminophenylarsinic acid, 2-*nitro*-5-*methyldiphenylamine*-6′-*arsinic acid* (V) was obtained. On reduction, the corresponding *dichloroarsine* (VI) was produced, and this on boiling in acetic acid solution was converted into 10-*chloro*-4-*nitro*-1-*methyl*-5 : 10-*dihydrophenarsazine*. The physical properties, melting points, solubilities and colour of these arsenic compounds are in agreement with the results described (this vol., *loc. cit.*) for the isomeric compounds.

EXPERIMENTAL.

5-*Amino*-2-*acetamidotoluene* (compare Morgan and Micklethwait, *loc. cit.*).—5-Nitro-2-acetamidotoluene (8 g.), mixed with alcohol (27·5 c.c.), water (27·5 c.c.), and acetic acid (2·75 c.c.), was treated at the boiling point with iron filings (11 g.), added cautiously in small portions. The mixture was boiled for 4 hours, the liquid filtered as hot as possible, and the residue well washed with alcohol. The alcohol was distilled off from the united filtrates, the residue mixed with water, and the boiling solution treated with decolorising charcoal. The filtrate deposited colourless crystals of 5-*amino*-2-*acetamidotoluene*, which, recrystallised from alcohol, yielded needles, m. p. 143° (Found in substance dried at 109° : N, 17·4. $C_9H_{12}ON_2$ requires N, 17·1%).

4-Nitro-3-aminotoluene was prepared by heating a mixture of 3 : 4-dinitrotoluene (115 g.), concentrated ammonia solution (284 c.c.), and methyl alcohol (1736 c.c.) in an autoclave at 150° for 6 hours (compare Kenner and Parkin, *loc. cit.*). After evaporating to dryness on the water-bath, the residue was crystallised from a little ethyl alcohol, 60 g. of pure nitroamine being obtained.

3-*Chloro*-4-*nitrotoluene*.—A suspension of finely divided 4-nitro-3-aminotoluene (15 g.) in hydrochloric acid (17 c.c.) and water (34 c.c.) was diazotised below 0° with a solution of sodium nitrite (7·5 g.) in water (10 c.c.). The diazo-solution was poured with stirring but without cooling into a solution of cuprous chloride (8·5 g.) in hydrochloric acid (29 c.c.). After warming on the water-bath for a short time, the chloronitrotoluene was distilled in steam, extracted with ether, washed with sodium hydroxide solution and with water, dried with calcium chloride, and the ether evaporated. The residue was distilled; 9·9 g. passed over at 146°/19 mm. and solidified on cooling to a mass of pale yellow needles, m. p. 22°.

3-*Bromo*-4-*nitrotoluene* (II).—A suspension of finely divided 4-nitro-3-aminotoluene (30 g.) in hydrobromic acid (36%; 81 c.c.) and water (54 c.c.) was treated below 0° with a solution of sodium nitrite (14·1 g.) in water (24 c.c.). The diazo-solution was added with stirring but without cooling to a solution of cuprous bromide in hydrobromic acid (*d* 1·49; 67 c.c.). The cuprous bromide was prepared by saturating with sulphur dioxide a solution prepared by mixing solutions of copper sulphate crystals (36·2 g.) in water (120 c.c.) and potassium bromide (18·2 g.) in water (42 c.c.). The *product* (23 g.) was isolated as described for 3-chloro-4-nitrotoluene. It formed yellow needles, m. p. 37°, b. p. 156—158°/19 mm. It is readily soluble in alcohol and ether but insoluble in water (Found : Br, 37·1. $C_7H_6O_2NBr$ requires Br, 37·0%).

3-*Iodo*-4-*nitrotoluene*.—A solution of potassium iodide (24·5 g.) in water (41 c.c.) was added slowly to the diazo-solution prepared from 4-nitro-3-aminotoluene (14·5 g.), sulphuric acid (11 c.c.) and water (102 c.c.), and a solution of sodium nitrite (8·2 g.) in water (16·3 c.c.). Nitrous fumes were evolved and solid matter containing iodine separated. After standing at the ordinary temperature for 15 minutes, the liquid was heated on the water-bath for an hour and a little sodium bisulphite was added to remove the excess of iodine. Since the semi-solid product was not readily volatile in steam, it was cooled, filtered off, and dissolved in ether, and the ethereal solution was worked up as described for the analogous chloro-compound. On evaporation of most of the ether, the *iodonitrotoluene* crystallised in orange-coloured needles, which were pressed on porous porcelain and recrystallised from alcohol; the orange-yellow needles thus obtained melted at 95—97° to a milky liquid, which became clear at 104°; after resolidification, this melted at 103—105° without any preliminary change (Found : I, 47·7. $C_7H_6O_2NI$ requires I, 48·25%). Beilstein and Kuhlberg (*loc. cit.*) give the melting point of the nitration product of *m*-iodotoluene as 108—109°.

Nitration of 3-*Bromo*-5-*acetotoluidide*.—(*a*) The acetyl derivative (10 g.) was added in small quantities to cold nitric acid (*d* 1·5; 30 c.c.) so that the temperature remained between 0° and 10°. The clear yellow solution was kept in cold water for 20 hours and then poured on ice (150 g.). The precipitated solid, after crystallising from alcohol, appeared from analysis to be impure dinitro-compound. (*b*) The acetyl derivative (10 g.) was recovered unchanged when it was added to nitric acid (*d* 1·45; 30 c.c.) below 0°, and the mixture poured on ice after 10 minutes.

3-*Chloro*-2-*nitrotoluene*.—A suspension of finely divided 2 : 3-dinitro-4-aminotoluene (11 g.) in hydrochloric acid (80 c.c.) and alcohol (80 c.c.) was treated below 0° with a solution of sodium nitrite (9 g.) in water (10 c.c.). The liquid was heated on the water-bath : when the temperature reached 15°, nitrogen and acetaldehyde were freely evolved; at 45°, the liquid had a deep red colour; at 70°, all reaction was over, the colour of the solution changed to pale orange-yellow, and a heavy dark-coloured oil was precipitated.

A yellow oil passed over on steam distillation. This was extracted in ether, washed with a solution of sodium hydroxide and with water, and dried with calcium chloride, and the ether evaporated. The residue (moderate yield), which crystallised on cooling, was pressed on porous porcelain; it then had m. p. 21—22° (Found : Cl, 20·7; N, 8·3. Calc. : Cl, 20·7; N, 8·2%).

3-*Bromo*-2-*nitrotoluene* (I).—This was prepared in a similar manner to the preceding substance, 2 : 3-dinitro-4-aminotoluene (48 g.), hydrobromic acid (*d* 1·324; 700 c.c.), alcohol (350 c.c.), sodium nitrite (39·3 g.), and water (70 c.c.) being used. When the diazo-solution was heated on the water-bath, traces of a lachrymatory substance were evolved. 3-*Bromo*-2-*nitrotoluene* has b. p. 129—130°/10 mm. and m. p. 27°. It crystallises in pale yellow needles, somewhat soluble in alcohol and ether, but insoluble in water (Found: N, 6·4; Br, 37·5. $C_7H_6O_2NBr$ requires N, 6·5; Br, 37·0%). On oxidation with potassium permanganate in neutral solution it was converted into a bromonitrobenzoic acid, m. p. 249—253°, which was doubtless 3-bromo-2-nitrobenzoic acid, since this is the only one of the known nine isomerides which melts above 200°. The unknown tenth bromonitrobenzoic acid corresponds to 6-bromo-2-nitrotoluene, from which the new bromonitrotoluene was shown to be different.

The residue in the distillation flask after the removal of the bromonitrotoluene under reduced pressure solidified on cooling and crystallised well from alcohol (charcoal). After three crystallisations, it was obtained in pale yellow prisms with a faint green reflex and had m. p. 95—96°, unchanged after further recrystallisation from ligroin (b. p. 60—80°) (Found: C, 30·1; H, 2·0; N, 5·7, 5·75; Br, 50·1, 49·7. $C_{12}H_9O_4N_2Br_3$ requires C, 29·7; H, 1·9; N, 5·8; Br, 49·5%). The constitution of this apparently homogeneous substance is unknown.

4-*Bromo*-2 : 6-*dinitrotoluene*.—The diazo-solution prepared from 2 : 6-dinitro-4-aminotoluene (26 g.), hydrobromic acid (36%; 54 c.c.), water (36 c.c.), and sodium nitrite (9·4 g.) in water (16 c.c.) was added to a solution in hydrobromic acid (*d* 1·49; 44·5 c.c.) of cuprous bromide prepared as above from copper sulphate crystals (24·1 g.) in water (80 c.c.) and potassium bromide (12·1 g.) in water (28 c.c.). The reaction was carried out in a large beaker because of the excessive frothing, which is difficult to control. The *product* was heated on the water-bath for a short time, water added and, after cooling, the solid matter was filtered off, washed with water, and recrystallised from alcohol. After two crystallisations, it was obtained in orange-yellow needles, m. p. 89—90° (Found : N, 10·9; Br, 30·1. $C_7H_5O_4N_2Br$ requires N, 10·7; Br, 30·6%).

Attempts to prepare 3-Bromo-4-nitrotoluene from 3 : 4-*Dinitro- and* 4 : 5-*Dinitro-2-aminotoluenes*.—These dinitrotoluidines (11 g.) were treated as described for 2 : 3-dinitro-4-aminotoluene. In the case of the former, a small quantity of a pale yellow oil was obtained which partly solidified on cooling. After being pressed on porous porcelain, the solid had m. p. 31—32°. In admixture with 3-bromo-4-nitrotoluene, it melted at a somewhat higher temperature, showing that it was a slightly impure specimen of this substance. From 4 : 5-dinitro-2-aminotoluene, a little oil was obtained which solidified in a freezing mixture. It liquefied at 15°, but the quantity was too small for fractional solidification.

2-*Nitro*-5-*methyldiphenylamine*-6′-*arsinic Acid* (V).—A mixture of 3-bromo-4-nitrotoluene (16·7 g.), *o*-aminophenylarsinic acid (16·7 g.), potassium carbonate (13·4 g.), amyl alcohol (78 c.c.), and a trace of copper powder was boiled for 5 hours. Volatile products were removed by steam distillation, the aqueous solution was treated with decolorising charcoal and filtered, and the filtrate acidified. The precipitated *acid*, crystallised twice from dilute acetic acid (charcoal), gave golden-yellow needles, m. p. 228—230° (decomp.), in moderate yield (Found: As, 21·6. $C_{13}H_{13}O_5N_2As$ requires As, 21·3%).

2-*Nitro*-5-*methyldiphenylamine*-6′-*dichloroarsine* (VI).—The preceding substance (2·2 g.), dissolved in a hot mixture of alcohol (11 c.c.) and hydrochloric acid (11 c.c.) containing a trace of iodine, was reduced by passage of sulphur dioxide for a few minutes. An oil was precipitated which partly solidified on cooling. It was extracted with benzene and the extract was washed with concentrated hydrochloric acid, dried with calcium chloride, and evaporated to small bulk. When the residue cooled, the *dichloroarsine* was deposited in orange-red needles, m. p. 137° (slight decomp.) (Found: Cl, 18·6. $C_{13}H_{11}O_2N_2Cl_2As$ requires Cl, 19·0%). The mother-liquor furnished a further quantity of slightly impure material, which, however, was suitable for the following preparation.

10-*Chloro*-4-*nitro*-1-*methyl*-5 : 10-*dihydrophenarsazine* (VII).—The preceding substance (1 g.) was boiled in acetic acid solution (10 c.c.) for 2 hours. Hydrogen chloride was evolved and red solid material separated. Acetic acid was added until a homogeneous solution at the boiling point was obtained. On cooling, 10-*chloro*-4-*nitro*-1-*methyl*-5 : 10-*dihydrophenarsazine* was deposited in deep red needles, m. p. 198—200° (slight decomp.) (Found: Cl, 10·3. $C_{13}H_{10}O_2N_2ClAs$ requires Cl, 10·5%).

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