Anal. Calcd. for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 70.29; H, 7.23.

dl-**3-Ethylenedioxy-14β-pregn-5-ene-11,16,20-trione (XII).**—Hydroxylation of 2β,4b-dimethyl-1α-carbomethoxymethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4-one[1] (XI, 1.45 g.) with osmium tetroxide by the procedure described for I provided 600 mg. of glycol ester, m.p. 143–155°, along with 720 mg. of crystalline glycol acid. Cleavage of the glycol ester with periodic acid gave 579 mg. of 2β,4b-dimethyl-1α-carbomethoxymethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4-one, m.p. 139–142°. Recrystallization from benzene–petroleum ether raised the melting point to 144°.

Anal. Found: C, 68.87; H, 8.08.

The Claisen ring closure procedure used with II converted 540 mg. of the above 1α-carbomethoxymethyl isomer to 400 mg. (80%, first crop from ethyl acetate–ether) of *dl*-3-ethylenedioxy-14β-pregn-5-ene-11,16,20-trione (XII) melting at 210–214°. A sample recrystallized from ethanol had m.p. 213.5–215°, λ_{max} 286 mμ, ϵ_{mol} 7,900, and gave a violet color with alcoholic ferric chloride.

Anal. Found: C, 71.74; H, 8.12.

dl-**3-Ethylenedioxy-14β-pregn-5-ene-11,20-dione (XIV) and** *dl*-**11-Keto-14β-progesterone (XV).**—Procedures essentially identical to those employed in the natural series were used.

From 289 mg. of XII there was obtained 353 mg. (88%) of the 16-enol tosylate XIII melting at 155–175°. Recrystallizations from chloroform–methanol and benzene gave m.p. 198–200°; λ_{max} 5.86, 5.97, 6.05, 6.22 μ.

Anal. Found: C, 67.04; H, 6.61.

Hydrogenolysis–hydrogenation of 180 mg. of the tosylate XIII afforded 86 mg. (69%, first crop from methanol) of *dl*-3-ethylenedioxy-14β-pregn-5-ene-11,20-dione (XIV) which melted at 166–170°. The analytical sample melted at 171–172.5° after recrystallization from ethyl acetate; λ_{max} 5.86, 9.05 μ. The infrared solution spectrum ($CHCl_3$) was different from that of compound IX beyond 6 μ.

Anal. Found: C, 74.07; H, 8.78.

Hydrolysis of 55 mg. of XIV was carried out in 1 ml. of tetrahydrofuran with 0.5 ml. of 3 *N* perchloric acid at room temperature for 3.5 hours. Crystallization of the product from benzene–petroleum ether afforded 41 mg. of *dl*-11-keto-14β-progesterone (XV), m.p. 151–153°. After recrystallization from ethyl acetate and ether–petroleum ether, XV had m.p. 153° and 168°; $\lambda_{max}^{CHCl_3}$ 5.86, 6.0, 6.17 μ.

Anal. Found: C, 76.85; H, 8.40.

dl-**3-Ethylenedioxy-13α-pregn-5-ene-11,16,20-trione (XVII).**—The experimental procedures used for the conversion of I to III were used.

A. **Esterification.**—Potassium carbonate–methyl iodide was used to esterify 2α,4b-dimethyl-1β-carboxymethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4α-ol (XVI)[1] in acetone. The product was recrystallized from ethyl acetate–ether petroleum ether and melted at 138–139°; λ_{max} 2.93, 5.82, 6.05 μ.

B. **Oxidation.**—Chromic anhydride–pyridine converted the above 4α-hydroxy methyl ester to 2α,4b-dimethyl-1β-carbomethoxymethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4-one, m.p. 125–126°; λ_{max} 5.76, 5.87, 6.05 μ.

Anal. Found: C, 72.28; H, 8.48.

C. **Hydroxylation.**—Reaction of the above keto methyl ester with osmium tetroxide afforded the mixture of glycols, 2α,4b-dimethyl-1β-carbomethoxymethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4-one. A portion recrystallized from ethyl acetate had m.p. 172–174°; λ_{max} 2.95, 5.76, 5.88 μ.

Anal. Found: C, 66.63; H, 8.97.

D. **Cleavage.**—Periodate cleavage of the crude glycol mixture gave 2α,4b-dimethyl-1β-carbomethoxymethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4-one, m.p. 108–109°; λ_{max} 5.78, 5.82 μ.

Anal. Found: C, 68.74; H, 8.23.

E. **Ring Closure.**—The above acetonylacetic ester was cyclized in the presence of sodium methoxide. The product, *dl*-3-ethylenedioxy-13α-pregn-5-ene-11,16,20-trione (XVII), was recrystallized from ethyl acetate and melted at 226–229°; λ_{max} 285 mμ, ε 9,100; $\lambda_{max}^{pH\ 1}$ 287 mμ, ε 9,100; $\lambda_{max}^{pH\ 13}$ 303 mμ, ε 19,500; λ_{max} 5.85, 6.07, 6.17 μ.

Anal. Found: C, 71.21; H, 7.53.

dl-**3-Ethylenedioxy-13α-pregn-5-ene-11,20-dione (XIX) and** *dl*-**11-Keto-13α-progesterone (XX).**—Reaction of XVII with *p*-toluenesulfonyl chloride in pyridine proceeded to give 16-enol tosylate XVIII. After recrystallization from ethyl acetate, XVIII had m.p. 189–190°; λ_{max} 5.82, 5.97, 6.09, 6.22 μ.

Anal. Found: C, 66.44; H, 6.69.

Palladium–barium carbonate hydrogenation of XVIII gave a mixture which consisted of starting material, colored side products and, by chromatography, about 5% of *dl*-3-ethylenedioxy-13α-pregn-5-ene-11,20-dione (XIX), m.p. 142–145°; λ_{max} 5.87, 9.0 μ.

Acid hydrolysis of XIX gave *dl*-11-keto-13α-progesterone, m.p. 153–158°; λ_{max} 5.88, 5.97, 6.17 μ.

RAHWAY, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

Derivatives of Indole, 6-Amino-3-indoleacetic Acid[1]

BY R. K. BROWN AND R. A. GARRISON

RECEIVED JANUARY 25, 1955

6-Nitrogramine methiodide reacts more readily than does 6-nitrogramine itself with aqueous potassium cyanide in a buffered solution to produce 6-nitro-3-indoleacetonitrile. Removal of the nitrile from the aqueous phase by an organic phase as soon as it is formed increases the yield of the product. Hydrolysis of the nitrile to the carboxylic acid required concentrated hydrochloric acid. Raney nickel and hydrogen converted both 6-nitro-3-indoleacetonitrile and 6-nitro-3-indoleacetic acid to the corresponding amines.

The well known plant growth stimulating property of 3-indoleacetic acid along with the obvious structural similarity between 6-aminoindole[2] and the carcinogens 2-aminofluorene[3] and 3-aminodibenzothiophene[4] prompted interest in the preparation of 6-amino-3-indoleacetic acid. Although 3-indoleacetic acid itself fails to induce tumor growth,[5] the incorporation of the amino moiety in the aromatic ring may well yield a compound possessing interesting physiological properties.

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(1) Taken in part from a thesis submitted by R. A. Garrison in partial fulfillment of the requirements for the M.Sc. degree, Department of Chemistry, University of Alberta.

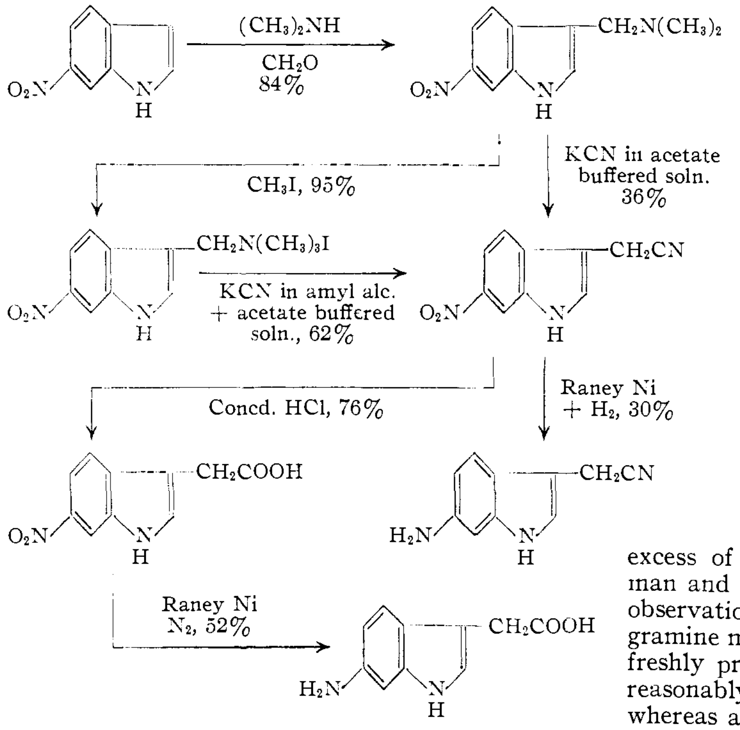
(2) R. K. Brown and N. A. Nelson, THIS JOURNAL, **76**, 5149 (1954).

(3) R. H. Wilson, D. DeEds and A. J. Cox, *Cancer Research*, **1**, 595 (1941).

(4) E. C. Miller, J. A. Miller, R. B. Sandin and R. K. Brown, *ibid.*, **9**, 504 (1949).

(5) M. J. Shear and J. Leiter, *J. Natl. Cancer Inst.*, **2**, 241 (1941).

The route which eventually gave 6-amino-3-indoleacetic acid is shown in the accompanying diagram and involves the alkylation of a cyanide[6-8] with the Mannich base 6-nitro-3-dimethylaminomethylindole (6-nitrogramine).



The Mannich base, 6-nitrogramine, was obtained by slight modifications of published procedures[6,9] but required less time and lower reaction temperatures than did gramine itself. In fact, usual temperatures and extended reaction time resulted in lower yield. Furthermore, dilute ammonium hydroxide rather than the usual caustic solution was employed to liberate the 6-nitrogramine from the acidic reaction mixture to minimize undesirable side reaction. Indeed, when 6-nitrogramine was warmed with dilute aqueous sodium hydroxide (0.01 *N*) the evolution of dimethylamine was pronounced, indicating decomposition of the Mannich base. From the reaction mixture was isolated a material analyzing for 6,6′-dinitro-3,3′-diindolylmethane. However, the use of the dilute ammonium hydroxide to free the 6-nitro-3-dimethylaminomethylindole did not completely eliminate similar decomposition since from one preparation of the Mannich base there was isolated a small quantity of material identical with the 6,6′-dinitro-3,3′-diindolylmethane obtained from the dilute caustic reaction. Snyder and Eliel[10] have reported a similar type of self-condensation of N-methylgramine methiodide in refluxing aqueous alkali to produce 1,1′-dimethyl-3,3′-diindolylmethane. They also obtained the latter compound from a mixture of N-methylindole and formalin in acetic acid.

Purification of 6-nitrogramine by crystallization from diluted alcohol is satisfactory, in spite of the obvious odor due to liberation of dimethylamine, providing excessive heating of the alcohol solution is avoided. However, when it was found that a quantity of 6-nitrogramine of melting point 175–177° heated one hour in alcohol and subsequently crystallized by dilution with water melted at 165–170°, this route for purification was abandoned. The method of reprecipitation of the base from dilute hydrochloric acid by ammonium hydroxide was found to be rapid and highly satisfactory.

The method of alkylation of potassium cyanide by gramine as described by Snyder and Pilgrim[8] when applied to 6-nitrogramine failed to give the expected nitrile yielding instead, in a number of attempts, only a dark insoluble material from which no satisfactory compound could be obtained. Since the cationoid activity of gramine methiodide has been found to exceed that of gramine itself,[6,11-13] 6-nitrogramine methiodide was prepared using a large excess of methyl iodide as advocated by Geissman and Armen.[12] In agreement with published observations on gramine methiodide, the 6-nitrogramine methiodide was found to be unstable. The freshly prepared quaternary ammonium salt gave reasonably good values for carbon and hydrogen, whereas a duplicate analysis on the same material kept for 48 hours showed marked deviation from the calculated values. Alkylation of potassium cyanide with 6-nitrogramine methiodide was attempted following established procedures[8] but here again only a product of polymeric nature was obtained. However, in one of the attempts a small amount of material analyzing for 6-nitro-3-indoleacetamide was isolated.

The nitrile eventually was synthesized in 36% yield by the alkylation of potassium cyanide with 6-nitrogramine in an aqueous solution of sodium acetate and acetic acid buffered to a *p*H range of 4.5–5.5. Recently Leeté and Marion[14] successfully obtained 3-hydroxymethylindole from gramine methiodide by avoiding self-condensation of the 3-hydroxymethylindole in the alkaline solution to 3,3′-diindolylmethane by a two-phase reaction mixture in which the alcohol was removed from the alkaline aqueous phase with ether as soon as it was formed. In a similar manner using as the organic phase *n*-amyl alcohol, a better solvent for 6-nitro-3-indoleacetonitrile than is ether, the 6-nitrogramine methiodide was shaken with aqueous potassium (or sodium) cyanide and gave the nitrile in 26% yield. A combination of the two-phase system with buffered aqueous phase gave 62% yield of 6-nitro-3-indoleacetonitrile.

Dilute acid hydrolysis gave only unchanged nitrile, whereas a one-hour reflux in concentrated hydrochloric acid converted 6-nitro-3-indoleaceto-

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(6) H. R. Snyder, C. W. Smith and J. M. Stewart, This Journal, **66**, 200 (1944).

(7) H. R. Snyder and E. L. Eliel, *ibid.*, **70**, 1703 (1948).

(8) H. R. Snyder and F. J. Pilgrim, *ibid.*, **70**, 3770 (1948).

(9) H. Kühn and O. Stein, *Ber.*, **70**, 567 (1937).

(10) H. R. Snyder and E. L. Eliel, This Journal, **71**, 663 (1949).

(11) H. R. Snyder and C. W. Smith, *ibid.*, **66**, 350 (1944).

(12) T. A. Geissman and A. Armen, *ibid.*, **74**, 3916 (1952).

(13) C. Schöpf and J. Thesing, *Angew. Chem.*, **63**, 377 (1951).

(14) E. Leeté and L. Marion, *Can. J. Chem.*, **31**, 775 (1953).

nitrile to the carboxylic acid in 76% yield.

The 6-nitroindoleacetic acid was changed readily to the amine by newly prepared Raney nickel with hydrogen. A good yield can be obtained only by repeated extraction of the Raney nickel with hot methyl alcohol *and* by crystallizing the amino acid from *small* volumes of water.

The same method of reduction gave 6-amino-3-indoleacetonitrile from the corresponding nitro compound.

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Experimental

All melting points are corrected unless otherwise stated.

The 6-nitroindole required for this work was prepared from the directions given by Majima and Kotake.[15] In our hands the preparation of 3-carbethoxyindole by their method was unsatisfactory. Accordingly the essential features of the modified procedure are given below.

3-Carbethoxyindole.—The indolylmagnesium iodide was prepared as usual[16] in an adequate quantity of ether to prevent precipitation of the Grignard reagent when the solution was cooled to −15°. Addition of the ethereal ethyl chlorocarbonate was carried out so that the reaction temperature did not exceed −5°.[16] At the end of the reaction the ether solution was separated into its two layers. From the upper layer containing unreacted ethyl chlorocarbonate was recovered some indole as well as a small amount of 3-carbethoxyindole. The lower layer (decomposed carefully with *ice*) yielded the bulk of the carbethoxyindole as well as recoverable indole. Peroxide-free ether is advocated in these reactions to avoid undue production of impurities which markedly color the product. The total yield of 3-carbethoxyindole was 69% on the basis of the indole consumed.

Conversion of 3-carbethoxyindole to 6-nitroindole proceeded according to published directions.[15]

6-Nitro-3-dimethylaminomethylindole (6-Nitrogramine).—Twenty grams of 6-nitroindole in 60 ml. of glacial acetic acid was added slowly with stirring to a solution of 24 ml. of 25% aqueous dimethylamine and 12 ml. of 33% formalin in 20 ml. of acetic acid. The reaction mixture stood at 45–55° for 1.5 hours and was then diluted with water, cooled in ice and basified by slow addition of dilute ammonium hydroxide to the rapidly stirred solution. After 3 hours in a refrigerator the solid was removed, washed with water and air dried giving 25 g. of crude base melting at 167–173° (uncor.). Reprecipitation from a hydrochloric acid solution with dilute ammonium hydroxide afforded 22.6 g. (84%) of pure material, m.p. 178–180°.

Anal. Calcd. for $C_{11}H_{13}N_3O_2$: C, 60.2; H, 5.98. Found: C, 60.0; H, 6.0.

The hydrochloride precipitated from an ether solution of 6-nitrogramine melted sharply at 229–230° dec.

Anal. Calcd. for $C_{11}H_{14}N_3O_2Cl$: C, 51.7; H, 5.52. Found: C, 51.7; H, 5.52.

The picrate of 6-nitrogramine (from alcohol) melted at 198–200°.

Anal. Calcd. for $C_{17}H_{16}N_6O_9$: C, 45.5; H, 3.8. Found: C, 45.4; H, 3.7.

A small amount of solid (0.3 g.) insoluble in the dilute hydrochloric solution of 6-nitrogramine when thrice crystallized from diluted alcohol melted at 263–265° dec. and gave no depression of melting point when mixed with a sample of 6,6-dinitro-3,3′-diindolylmethane (see below).

6,6′-Dinitro-3,3′-diindolylmethane.—6-Nitrogramine (1 g.) in 200 ml. of 0.01 *N* aqueous caustic was heated on the steam-bath for 24 hours. The cooled solution precipitated a yellow solid which was dried and taken up in anhydrous ether. Addition of dry hydrogen chloride precipitated 0.4 g. of 6-nitrogramine hydrochloride. The ether filtrate was washed with water then with dilute sodium bicarbonate and subsequently dried over anhydrous sodium sulfate. Removal of the ether gave 0.17 g. of yellow solid melting at 263–265° dec. Crystallization from slightly diluted alcohol produced no change in melting point.

Anal. Calcd. for $C_{17}H_{12}N_4O_4$: C, 60.7; H, 3.6. Found: C, 60.6, 60.9; H, 3.8, 3.7.

The Methiodide of 6-Nitro-3-dimethylaminomethylindole.—To a quantity (8.5 g.) of 6-nitrogramine in 300 ml. of dry ethyl alcohol was added excess methyl iodide (12 ml.). A rise in temperature occurred and a solid appeared. The mixture was cooled and the solid obtained was washed with cold absolute alcohol and air-dried, m.p. 203–205° dec., yield 12.7 g. (95%). Attempts at further purification led only to decomposition. In fact, upon standing 48 hours, decomposition was detected by the odor of liberated dimethylamine, the decrease in melting point as well as progressively poorer carbon and hydrogen analyses. The freshly prepared material, air-dried for 2 hours and then kept 5 hours in a desiccator over phosphoric anhydride, gave a surprisingly good analysis.

Anal. Calcd. for $C_{12}H_{16}N_3O_2I$: C, 39.9; H, 4.5. Found: C, 39.2, 39.8, 39.5; H, 4.6, 4.8, 4.9.

6-Nitro-3-indoleacetamide.—The methiodide of 6-nitrogramine (2.7 g.) in 400 ml. of alcohol–water solution (1:1) was treated with an aqueous solution of 3.5 g. of potassium cyanide. The mixture was heated on the steam-bath for 30 hours and from the orange solution a marked evolution of dimethylamine was noted. The cooled solution deposited 0.45 g. of brown material from which no satisfactory material could be isolated. The filtrate, decolorized with charcoal and reduced to half its volume under diminished pressure, gave 0.55 g. of yellow material melting at 219–223° (uncor.). Four crystallizations from diluted alcohol gave 0.25 g. of fine, yellow needles melting sharply with decomposition at 239–240°, yield 15%.

Anal. Calcd. for $C_{10}H_9N_3O_3$: C, 54.8; H, 4.2. Found: C, 54.8, 55.0; H, 4.2, 4.2.

6-Nitro-3-indoleacetonitrile.—The 6-nitrogramine methiodide (10 g.) was mixed with 300 ml. of *n*-amyl alcohol and 300 ml. of sodium acetate–acetic acid buffered solution (6 g. of acetic acid and 8.2 g. of sodium acetate per liter). Sodium cyanide (10 g.) was added and the mixture heated to 75° in a thick-walled vessel and then vigorously shaken. After two hours, the alcohol layer was removed, washed with water and distilled with steam to eliminate the alcohol. The hot water from the steam distillation flask when filtered and cooled deposited a light yellow substance. Several hot water extractions using in each case the mother liquor from the previous extraction, produced further quantities of the material. One recrystallization from water gave 3.45 g. of yellow crystals melting at 153–154°, yield 62%.

Anal. Calcd. for $C_{10}H_7N_3O_2$: C, 59.7; H, 3.5. Found: C, 59.6, 59.2; H, 4.0, 3.7.

6-Nitro-3-indoleacetic Acid.—6-Nitro-3-indoleacetonitrile (6 g.) in 400 ml. of concd. hydrochloric acid was refluxed for one hour. The cold solution gave a precipitate which was dissolved in 75 ml. of water containing sufficient sodium carbonate. After treatment with charcoal and filtration, the solution was acidified carefully with concd. hydrochloric acid and afforded 5 g. (76%) of orange material, m.p. 212–214° dec. Reprecipitation did not alter the melting point.

Anal. Calcd. for $C_{10}H_8N_2O_4$: C, 54.6; H, 3.7. Found: C, 54.2; H, 3.8.

6-Amino-3-indoleacetic Acid.—6-Nitro-3-indoleacetic acid (5 g.) was reduced in methanol (200 ml.) with 2 g. of freshly prepared Raney nickel[17] and hydrogen (40 p.s.i.) in a Parr low pressure hydrogenation apparatus. Disappearance of the yellow color indicated complete reduction of the nitro group. The alcohol was separated and the Raney nickel repeatedly extracted with hot methanol. The combined alcohol extracts were decolorized and the alcohol removed under vacuum. The solid was taken up in hot water (decolorized again if necessary) and the water reduced in volume. Cooling deposited 2.3 g. (52%) of almost colorless material, m.p. 184–185° dec.

Anal. Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.1; H, 5.3. Found: C, 63.3; H, 5.2.

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[15] R. Majima and M. Kotake, *Ber.*, **63**, 2237 (1930).

[16] F. K. Signaigo and H. Adkins, THIS JOURNAL, **58**, 1122 (1936). A low temperature minimizes reaction at the nitrogen atom of indole.

[17] L. W. Covert and H. Adkins, *ibid.*, **54**, 4116 (1932).

The amine (0.4 g.) was acetylated by the method of Lumière and Barbier[18] and gave 0.42 g. of solid (86%) melting at 223–225° dec. An analytical sample crystallized from diluted alcohol melted at 224–225° dec.

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.1; H, 5.2. Found: C, 61.8; H, 5.1.

6-Amino-3-indoleacetonitrile.—The 6-nitro-3-indoleacetonitrile (1.2 g.) was reduced in methanol (100 ml.) with Raney nickel (1 g.) and hydrogen (40 p.s.i.). When the solution had become colorless the alcohol was filtered free from nickel and the latter thoroughly extracted with hot methanol. The combined alcohol extracts were decolorized and reduced under vacuum to 10 ml. Addition of water to incipient cloudiness followed by cooling gave 0.3 g. (30%) of brownish-gray crystals melting at 123–124.5°.

Anal. Calcd. for $C_{10}H_9N_3$: C, 70.2; H, 5.3. Found: C, 70.3; H, 5.2.

ALBERTA, CANADA

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[18] A. Lumière and H. Barbier, *Bull. soc. chim.*, **33**, 783 (1905).

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY OF CORNELL UNIVERSITY]

Dinitrobiphenyls Obtained by the Gomberg–Bachmann Reaction: A Quantitative Study[1]

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The Gomberg–Bachmann reaction of 3-nitrobenzenediazonium chloride with nitrobenzene and sodium acetate gives 3,X′-dinitrobiphenyls (and tar). The ratio of isomers produced 3,2′:3,3′:3,4′ is 31:25:44. Similar results were obtained with 4-nitrobenzenediazonium chloride.

Recently several groups of workers have reported quantitative studies of the orientation occurring in aromatic substitution by free-radical processes.[3] In the Gomberg–Bachmann reaction of nitrobenzene with benzenediazonium chloride and alkali, for example, 2-, 3- and 4-nitrobiphenyl are produced in a total yield of about 25% and a ratio of isomers of about 55:15:30. The task of obtaining reliable quantitative data of this sort requires a separate analytical procedure to be worked out for each example that is to be studied. Since we required samples of the six isomeric "symmetrical" dinitrobiphenyls and methods for their determination for another problem, we decided to determine the composition of the dinitrobiphenyl mixtures obtained by the Gomberg–Bachmann reaction of nitrobenzene with the diazonium salts derived from 3-nitroaniline and from 4-nitroaniline.

The examples of the Gomberg–Bachmann reaction carried out in this work involved the following reaction conditions: the filtered diazonium solution was treated with an excess of sodium acetate to give a solution containing approximately 0.9 *M* diazonium ions. This solution was stirred vigorously with about twice its volume of nitrobenzene. The dinitrobiphenyl fraction was isolated by removing the nitrobenzene under reduced pressure followed by two distillations of the dinitrobiphenyl residue with superheated steam. The isomer ratio was determined by the use of ultraviolet and infrared spectrophotometry.

The results (summarized in Table I) indicate that more *meta* and *para* substitution is occurring with the nitrobenzenediazonium compounds than was observed with benzenediazonium chloride[3a,b] or with *p*-bromo- and *p*-methylbenzenediazonium salts. There is not sufficient information at present to permit a decision whether the difference in orientation ratios is due to the nitro substituents or whether it arises from the use of sodium acetate in the Gomberg–Bachmann reaction with the nitro-compounds and sodium hydroxide with the others.

TABLE I

DINITROBIPHENYLS FROM THE GOMBERG–BACHMANN REACTION OF 3- AND 4-NITROBENZENEDIAZONIUM CHLORIDE WITH NITROBENZENE IN THE PRESENCE OF SODIUM ACETATE

Diazonium salt from	Yield of dinitrobiphenyl, % relative (actual)		
3-Nitroaniline	3,2′	3,3′	3,4′
	29.5(5)	25 (4)	45(8)
	32 (7)	24.5(6)	43(9)
Av.[a,c]	31 ± 2	25 ± 1	44 ± 1
4-Nitroaniline	4,2′	4,3′	4,4′
	35(7)	26(5)	39(7)
	31(7)	25(5)	42(9)
	36(14)	18(7)	48(18)
Av.[b,c]	34 ± 5	23 ± 3	43 ± 3

[a] Determined by ultraviolet spectrophotometry. [b] Determined by infrared spectrophotometry. [c] The standard deviations are larger than is calculated from the deviations of the individual values from their average since a conservative estimate of the spectrophotometric errors also is taken into account.

Experimental[4]

2,4′-Dinitrobiphenyl and 4,4′-Dinitrobiphenyl.—These compounds were obtained from the Eastman Kodak Co. They were recrystallized from absolute ethanol and from acetone, respectively. The 4,4′-isomer was obtained in the form of colorless needles, m.p. 228–233°,[5a] and the 2,4′-isomer as almost colorless needles, m.p. 92.7–93.7°.[5b]

2,2′-Dinitrobiphenyl.—This was obtained by the Ullmann reaction on *o*-chloronitrobenzene[6] in the form of pale yellow needles from absolute ethanol, m.p. 124–124.5°.

3,3′-Dinitrobiphenyl.—This compound was obtained by the reductive coupling of diazotized *m*-nitroaniline by an

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[1] Presented before the Division of Organic Chemistry at the 122nd A.C.S. Meeting, Atlantic City, N. J., September, 1952.

[2] Department of Chemistry, University of South Carolina, Columbia, S. C.

[3] See for example (a) D. R. Augood, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 2094 (1952); 44 (1953); (b) D. F. DeTar and H. J. Scheifele, THIS JOURNAL, **73**, 1442 (1951); (c) R. L. Dannley and M. Sternfeld, *ibid.*, **76**, 4543 (1954).

[4] All melting points are corrected.

[5] (a) G. Schultz, *Ann.*, **174**, 221 (1874); (b) R. Fittig, *ibid.*, **124**, 276 (1862).

[6] R. C. Fuson and E. A. Cleveland, *Org. Syntheses*, **20**, 45 (1940).