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]

By DeLos F. DeTar[2] and Abdul A. Kazimi

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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 nitrocompounds 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).

ammoniacal cuprous solution.[7] On recrystallization from acetone five times it was obtained as pale yellow plates, m.p. 201–202°.

2,3′-Dinitrobiphenyl and 4,3′-Dinitrobiphenyl.—3-Nitrobiphenyl was obtained by the Gomberg–Bachmann reaction of diazotized *m*-nitroaniline and benzene[8,9] in the form of almost colorless plates from 95% hexane–5% benzene, m.p. 57–58°. This was nitrated with concentrated nitric acid and the more soluble 2,3′-isomer separated by extraction of the crude dinitrobiphenyl mixture with methanol. The 4,3′-isomer was recrystallized from acetone giving almost colorless needles, m.p. 188–188.5°; yield 5.8 g. of product melting at 185–188° from 15 g. of 3-nitrobiphenyl.

Attempts to obtain the 2,3′-isomer by crystallization from methanol or from various concentrations of acetic acid gave a chalky product melting about 100–110°. By use of ethyl alcohol fine colorless plates, m.p. 118–119.5°, were obtained.

Ultraviolet Spectra.—The ultraviolet absorption spectra of the dinitrobiphenyls in isoöctane are shown in Fig. 1; they were obtained with a Beckman model DU spectrophotometer. Because of the insolubility of these compounds, the samples were first dissolved in methylene chloride and the solution diluted with isoöctane. For the quantitative runs *n*-heptane (purified by passage through a column of silica gel) was used, and the solvent thus contained 98% *n*-heptane and 2% methylene chloride by volume. The spectra are essentially the same in these two solvent mixtures.

The quantitative analyses of mixtures of 3,2′-, 3,3′- and 3,4′-dinitrobiphenyls used the following wave lengths: 230, 235, 240, 250, 270, 280, 290 mμ. The standard deviation for a single absorption reading was about 1% (relative). By carrying out a weighted least squares analysis for two sets of determinations of known mixtures it was found that the standard deviations of the spectrophotometric determinations of the isomers were as follows: 3,2′- 5.5%; 3,3′- 3%; 3,4′- 1% (relative).

***Infrared* Spectra.**[10]—These spectra were obtained with a Perkin–Elmer model 21 spectrophotometer using sodium chloride optics. The characteristic nitro group frequencies[11] at 1520 and 1350 cm.$^{-1}$ are recorded in Table II. The absorption band near 850 cm.$^{-1}$ is also reported.

TABLE II

CHARACTERISTIC NITRO GROUP FREQUENCIES

Compound	Nitro group absorption,[a] cm.$^{-1}$		
2-Nitrobiphenyl	1534(1534)	1357	853(856)
3-Nitrobiphenyl	1538(1534)	1348	876(879)[c]
4-Nitrobiphenyl	1511(1527)	1357	857(858)
2,2′-Dinitrobiphenyl	1527(1529)	1357	863(854)
2,3′-Dinitrobiphenyl	1522	1350	853(853)[c]
2,4′-Dinitrobiphenyl	1524(1531)	1350	859(854)
3,3′-Dinitrobiphenyl	1529[b](1535)	1351	863(859)[c]
3,4′-Dinitrobiphenyl	1522(1531)	1350	858(857)
4,4′-Dinitrobiphenyl	1484[b](1526)	1320 very broad	849(853)

[a] The spectra were run on a solid film from the melt; figures in parentheses were obtained in solution in acetone. Data are not available for the 1350 band in acetone since the solvent is opaque near this frequency. [b] The characteristic absorption frequency is not clearly present in the solid film, though there is strong absorption over a broad area near the expected region. [c] There is a definite strong peak in the 850 region for most of the nitro compounds, but for these particular compounds the selection of one specific frequency is rather arbitrary.

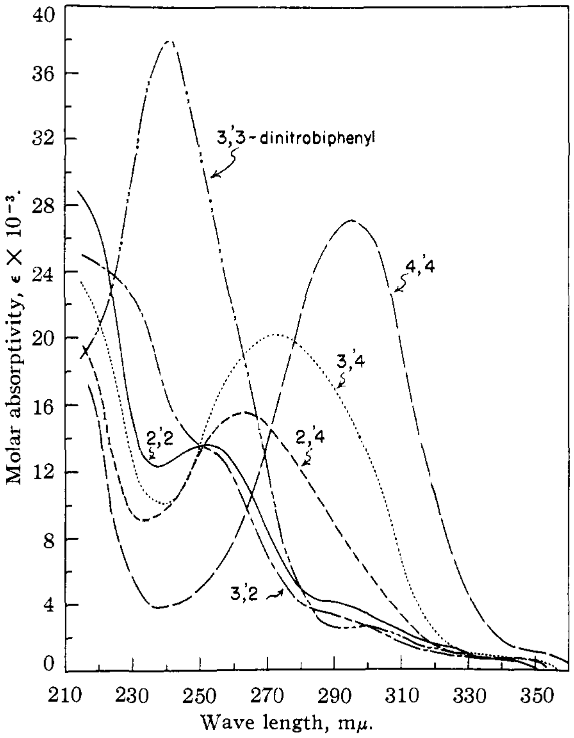

Fig. 1.—Ultraviolet absorption spectra of the symmetrical dinitrobiphenyls. Solvent: 2% CH_2Cl_2 in isoöctane, slit width 1 mm., Beckman DU spectrophotometer; $\epsilon = A/bc$ with A = absorbance (optical density), b = cell length (1.000 cm.), c = concn. in moles per liter.

The quantitative analysis of mixtures of 4,2′-, 4,3′- and 4,4′-dinitrobiphenyls utilized the following wave numbers in cm.$^{-1}$: 855, 849, 842, 782, 770, 742 and 732. Two solvents were used, acetone for the first two runs and carbon disulfide for the last one. The low solubility of the 4,3′- and the 4,4′-isomer in these solvents required the use of relatively thick cells, about 1 mm. path length, but even so the observed absorbance extended over an undesirably narrow range, the maximum absorbance available being about 0.2. Two procedures were used for obtaining the transmission values. In the first one the above region was scanned at 8 inches per micron. In the second procedure the required frequency was selected, the wave length drive clutch disengaged, and the absorption band scanned briefly so that demonstrable instrumental equilibrium had been established. The two scanning procedures gave the same results with these mixtures. The determination of an absorbance value requires three transmission values: 100%, 0% and *x*%. The 100% line was obtained by running pure solvent in the cell, the 0% by closing off the sample beam, and the *x*% by running the solution. Beer's law was valid within the accuracy of the data. The type of filling tube used for preparing samples of known concentration with these highly volatile solvents is shown in Fig. 2.

The Gomberg–Bachmann Reactions.—The same procedure was used for the first four runs reported in Table I. It is illustrated with a 3-nitroaniline run. 3-Nitroaniline (11.5 g.) was stirred with 27 ml. of concd. hydrochloric acid and diazotized at 1° with about 9 g. of sodium nitrite in 35 ml. of water. The solution was filtered, stirred vigorously with 200 ml. of nitrobenzene at 5–10°, and 26 g. of sodium acetate trihydrate in 33 cc. of distilled water was added. Stirring was continued for a total of 62 hours, the first three being at 5–10° and the remainder at room temperature. (This reaction time is unnecessarily long: see below.) For one run with each compound the sample of nitrobenzene was a student preparation which had been extracted with sodium carbonate solution several times, dried, and distilled under reduced pressure, this purification procedure being carried through twice. For a second run a commercial nitrobenzene was subjected to the same purification. There

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[7] E. R. Atkinson, C. R. Morgan, H. H. Warren and T. J. Manning, THIS JOURNAL, **67**, 1513 (1945).

[8] W. Blakey and H. S. Scarborough, *J. Chem. Soc.*, 3003 (1927).

[9] J. Elks, J. W. Haworth and D. H. Hey, *ibid.*, 1284 (1940).

[10] The infrared spectra of solid films of all six "symmetrical" dinitrobiphenyls have been deposited as Document number 4497 with the ADI Auxiliary Publication Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document numbers and by remitting in advance $1.25 for photoprints or $1.25 for 35 mm. microfilm by check or money order payable to Chief, Photoduplication Service, Library of Congress.

[11] R. R. Randle and D. H. Whiffen, *J. Chem. Soc.*, 4153 (1952).

seemed to be no great difference in the results obtained with two different nitrobenzene samples with any of the nitroanilines.

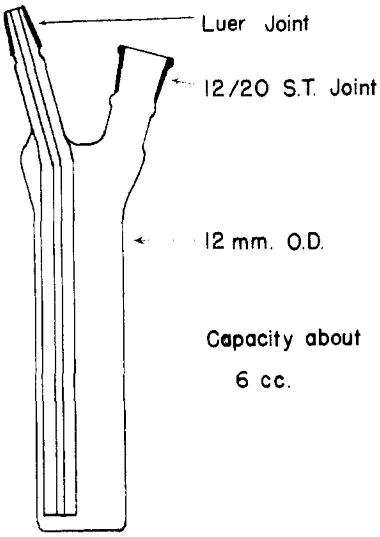

Fig. 2.—Sampling tube for quantitative infrared analyses. The sample is weighed into the tube directly or on a small aluminum foil boat; the volatile solvent, CS_2, acetone, etc., then is added and the tube weighed. Loss of solvent is prevented by a 12/20 plug and by a Luer cap, the latter being one of the standard Luer fittings obtainable from Becton, Dickinson and Co., Rutherford, N. J. The Luer joint fits the Perkin–Elmer cells and the sample transfer is effected by warming the upper part of the sampling tube with the hand. Designed by D. F. DeTar and V. Gold.

The isolation of the dinitrobiphenyl fraction was accomplished as follows: the nitrobenzene layer was separated, washed twice with water, dried over calcium chloride, and distilled under reduced pressure to remove most of the nitrobenzene. The tarry residue was transferred to a 300-ml. Kjeldahl flask using methylene chloride as a solvent, the solvent removed, and the residue subjected to distillation with superheated steam, the temperature of the steam just before entering the condenser was 175–185° (bath temperature about 220°). About 7 l. of distillate was collected, the last liter of which was clear and colorless. The first few hundred ml. containing a little nitrobenzene was discarded, the rest of the distillate was combined in a 12-l. flask and stirred several hours with 700 ml. of methylene chloride. The above steam-distillation procedure was then repeated, but only 5 l. of distillate needed to be collected. The residue in the Kjeldahl flask was negligible. It consisted of a slight film of tarry material which had carried over in the first distillation. The analysis was carried out on this dinitrobiphenyl mixture.

The last run reported in Table I was carried out somewhat differently. Crystalline 4-nitrobenzenediazonium chloride was prepared. Recrystallized 4-nitroaniline (6.90 g.) was dissolved in 25 cc. of glacial acetic acid (refluxing); dry hydrogen chloride was passed in, the mixture cooled at below 20° and 7 ml. of *n*-butyl nitrite added to the amine hydrochloride suspension. Addition of ether gave two layers. The upper ether layer was decanted and crystals obtained from the lower layer by successive additions of dimethylformamide and of ether. The resulting 5.2 g. of pale yellow hygroscopic diazonium salt was dissolved in water, treated with Norit, filtered, and diluted to 25 cc. Analysis of aliquots by precipitation of the azo compound with β-naphthol showed that 10 cc. contained 9.1 ± 0.2 mmoles of the diazonium salt. A 10-cc. aliquot was stirred with 50 cc. of purified nitrobenzene and a solution of 13.6 g. of sodium acetate trihydrate added at room temperature while the solution was vigorously stirred. After one hour it was no longer possible to obtain a color test for diazonium salt with β-naphthol. The *p*H of the solution was 5.7. The dinitrobiphenyl fraction was isolated by the general procedure described above except that phenolic material was extracted with sodium hydroxide. There was obtained 0.85 g. (38%) of dinitrobiphenyl fraction, 0.23 g. of alkali-soluble material, and 1.36 g. of material not volatile with superheated steam at 238° (temperature of vapors leaving steam-distillation flask).

COLUMBIA, SOUTH CAROLINA

[CONTRIBUTION FROM THE LABORATORY OF CHEMISTRY OF NATURAL PRODUCTS, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH]

Synthesis of 5,6-Dimethoxyindoles and 5,6-Dimethoxyoxindoles. A New Synthesis of Indoles

BY GORDON N. WALKER

RECEIVED NOVEMBER 20, 1954

5,6-Dimethoxyoxindole and 5,6-dimethoxyindoles have been synthesized by a new process involving low-pressure hydrogenation of 4,5-dimethoxy-2-nitrophenylacetic acid and 4,5-dimethoxy-2-nitrophenylacetonitriles, respectively, in the presence of palladium–charcoal. Evidence was found for formation of 2-aminoindoles as intermediates in hydrogenation of nitronitriles of this type. 3-Substituted oxindoles were prepared by condensation of 5,6-dimethoxyoxindole with aldehydes and subsequent hydrogenation. Hydrochlorides of 6-methoxybufotenine methyl ether and the corresponding 2-amino derivative, prepared by this method, produced a lowering of blood pressure in dogs.

The few reports of synthesis of dimethoxyindoles which have appeared have indicated that such compounds are not stable. Huebner and co-workers[1] very recently synthesized 5,6-dimethoxyindole by hydrogenation of 3,4-dimethoxy-6,β-dinitrostyrene and confirmed an earlier observation[2] that this indole is unstable. Similar lack of stability was noticed in other compounds[1] which were prepared by 3-substitution of the indole.

Since dimethoxyindoles are especially unstable in oxidizing environments, it was felt that a synthetic process involving reductive conditions would be favorable in preserving the indoles, once they were formed. The purpose of this report is to describe the successful development of a new synthesis of methoxyindoles and related oxindoles, based on palladium-catalyzed reduction of appropriate nitro-compounds.

Hydrogenation of nitro-ester I in ethyl acetate at room temperature in the presence of palladium–charcoal gave amino-ester II, but when acetic acid was used as solvent and the reaction carried out at 80°, ring closure to the oxindole III occurred. It

(1) C. F. Huebner, H. A. Troxell and D. C. Schroeder, THIS JOURNAL, **75**, 5887 (1953).

(2) A. E. Oxford and H. S. Raper, *J. Chem. Soc.*, 417 (1927).