Anal. Calcd for $C_{24}H_{23}N_5O_8$ (picrate): C, 56.58; H, 4.55; N, 13.75. Found: C, 57.13; H, 4.60; N, 13.73.

2,4-Dimethoxy-β-nitrostyrene (17). A mixture of 580 mg (5 mmol) of nitroenamine **1**, *m*-dimethoxybenzene (690 mg, 5 mmol), and trifluoroacetic acid (2.5 mL) was heated to 55–65 °C for 30 min. The dark purple mixture was than poured into ice water and extracted with methylene chloride and the organic layer was then washed with saturated $NaHCO_3$ and NaCl solution followed by drying (Na_2SO_4). Removal of solvent in vacuo yielded a semisolid which on trituration with methanol yielded 570 mg of **17** as yellow crystals. The mother liquor, which contained a mixture of compounds, was separated by column chromatography on silica gel (50 g). *m*-Dimethoxybenzene (141 mg, 24%) and 126 mg (18%) of **1** were recovered, together with 135 mg of **17**, affording a total of 705 mg (69%) of the desired product. Recrystallization from hot methanol gave yellow needles: mp 106–108 °C (lit.[15] mp 104 °C); IR ($CHCl_3$) 2950, 1600, 1495, 1325, 1260 cm^{-1}; NMR ($CDCl_3$) δ 3.86 (s, 3), 3.94 (s, 3), 6.50 (d, 1, J = 2 Hz), 6.57 (d of d, 1, J = 2, 8 Hz), 7.40 (d, 1, J = 8 Hz), 7.85 (d, 1, J = 13 Hz), 8.05 (d, 1, J = 13 Hz); UV (95% EtOH) 250 nm (ε 9230), 309 (sh, 6600), 366 (19 000).

2,4,5-Trimethoxy-β-nitrostyrene (18). This was prepared as described for **17**. Starting 1,2,4-trimethoxybenzene (64 mg, 18%) and 46 mg (18%) of nitroenamine **1** were recovered together with 178 mg (36%) of the desired **18** isolated after recrystallization from hot methanol as reddish-orange prisms: mp 132–133 °C (lit.[16] 132 °C); IR ($CDCl_3$) 2940, 2830, 1600, 1320, 1270 cm^{-1}; NMR ($CDCl_3$) δ 3.90 (s, 3), 3.95 (s, 3), 3.97 (s, 3), 6.55 (s, 1), 6.93 (s, 1), 7.81 (d, 1, J = 14 Hz), 8.19 (d, 1, J = 14 Hz); UV (95% EtOH) 245 nm (ε 8350), 265 (9200), 316 (7300), 396 (15 400).

2-Hydroxy-4,5-methylenedioxy-β-nitrostyrene (19). A mixture of 138 mg (1 mmol) of sesamol, 116 mg (1 mmol) of nitroenamine **1**, and trifluoracetic acid (0.5 mL) was heated at 40–55 °C for 15 min. The dark mixture was poured into ice water and extracted with ethyl acetate. The acidic aqueous solution was cooled overnight at 5 °C and 59 mg (mp 194–196 °C) of **19** crystallized as red needles. The organic phase was washed with saturated $NaHCO_3$ and NaCl solution and dried ($MgSO_4$). Removal of solvent yielded 150 mg of **19** as a red, amorphous solid. Recrystallization from ethyl acetate/hexane furnished small, red needles (mp 180–182 °C). Further recrystallization from 1 N HCl/methanol gave red needles (mp 200 °C). A quantitative yield of **19** was thus obtained: IR (Nujol) 3360, 1630, 1615, 1610, 1360, 1270 cm^{-1}; NMR (acetone-d_6) δ 6.03 (s, 2), 6.60 (s, 1), 7.17 (s, 1), 7.93 (d, 1, J = 14 Hz), 8.30 (d, 1, J = 14 Hz); UV (95% EtOH) 248 nm (sh, ε 7400), 270 (9300), 315 (5850), 405 (14 700); (1 M NaOH) 266 nm (ε 8400), 298 (4750), 345 (9100), 530 (21 700); reacidification with 1 M HCl gave the original spectrum; mass spectrum (70 eV) *m/e* (rel intensity) 209 (M^+, 29), 162 (100), 161 (39).

Anal. Calcd for $C_9H_7NO_5$: C, 51.68; H, 3.37; N, 6.70. Found: C, 51.79; H, 3.50; N, 6.40.

Acknowledgment. This work was supported by the National Institutes of Health (GM 09868).

Registry No.—**1**, 1190-92-7; **6**, 603-76-9; **7**, 61675-16-9; **8**, 1006-94-6; **9**, 61675-17-0; **10**, 3156-51-2; **12**, 2731-00-2; **13**, 61675-18-1; **14**, 61675-19-2; **15**, 61675-20-5; **16**, 61675-21-6; **16** picrate, 61675-22-7; **17**, 1891-10-7; **18**, 24160-51-8; **19**, 61675-23-8; 6-benzyloxyindole, 15903-94-3; indole, 120-72-9; 6-tosyloxyindole, 56596-14-6; *m*-dimethoxybenzene, 151-10-0; 1,2,4-trimethoxybenzene, 135-77-3; sesamol, 533-31-3.

References and Notes

(1) H. Lerche, D. König, and T. Severin, *Chem. Ber.*, **107**, 1499 (1974), and preceding papers.
(2) R. J. Sundberg, "The Chemistry of Indoles", Academic Press, New York, N.Y., 1970, and references cited therein.
(3) T. Severin and B. Brück, *Chem. Ber.*, **98**, 3847 (1965).
(4) M. Colonna and L. Marchetti, *Gazz. Chim. Ital.*, **97**, 533 (1967).
(5) E. H. A. Young, *J. Chem. Soc.*, 3493 (1958).
(6) R. V. Heinzelman, W. C. Anthony, D. A. Lyttle, and J. Szmuszkovicz, *J. Org. Chem.*, **25**, 1548 (1960).
(7) M. Ando, G. Büchi, and T. Ohnuma, *J. Am. Chem. Soc.*, **97**, 6880 (1975).
(8) J. Szmuszkovicz, Belgium Patent 621 047 (1963).
(9) K. T. Potts and J. E. Saxton, *Org. Synth.*, **40**, 68 (1960).
(10) This substance was first prepared by Dr. J. Belletire in this laboratory.
(11) M. Onda, M. Kawanishi, and M. Sasamoto, *J. Pharm. Soc. Jpn.*, **76**, 409 (1956).
(12) N. N. Bulatora and N. N. Suvorov, *Khim. Geterotsikl. Soedin.*, **5**, 813 (1969); *Chem. Abstr.*, **72**, 111212b (1969).
(13) J. Szmuskovicz, W. C. Anthony, and R. V. Heinzelman, *J. Org. Chem.*, **25**, 857 (1960).
(14) This substance was first prepared by Dr. M. Ando in this laboratory by another route.
(15) W. E. Cocker, T. B. H. McMurry, and P. A. Staniland, *J. Chem. Soc.*, 1034 (1965).
(16) J. Harley-Mason, *J. Chem. Soc.*, 200 (1953).

Synthesis of 4-Aminodiphenylamine and Its Relatives

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Received November 16, 1976

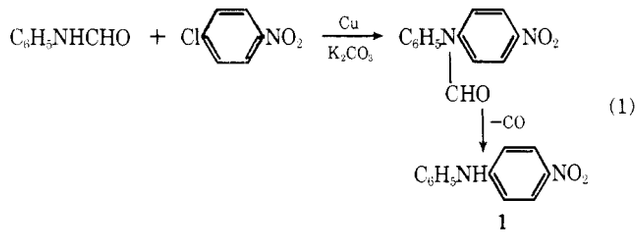
Formanilide is readily converted to its sodium salt by heating with metallic sodium or sodium hydride. Sodium formanilide condenses rapidly with *p*-nitrochlorobenzene in a high-boiling solvent at 150–165 °C. The condensation is further accelerated by addition of dimethylformamide. The product is 4-nitrodiphenylamine (1) (87–91% yield) which is readily hydrogenated to the title compound. Several other nitrodiphenylamines were prepared by this technique. *p*-Nitrobenzenediazonium bisulfate couples rapidly with diphenylamine in 25–30% sulfuric acid, but not so well in either weaker or stronger acid. The product is almost entirely 4-(4-nitrobenzeneazo)diphenylamine, which is readily hydrogenated to a separable mixture of the title compound and *p*-phenylenediamine.

p-Aminodiphenylamine and derived compounds have long been used as dye intermediates and as polymer stabilizers, for example, as antioxidants or antiozonants for elastomers. The following brief review of the literature shows the scope of the methods tried for their synthesis. The nitro and nitroso products are readily reduced to aminodiphenylamines.

A recent Russian review [1]of industrial processes concluded that the preferred process involves N-nitrosation of diphenylamine and Fischer–Hepp rearrangement to 4-nitrosodiphenylamine. These steps can be combined by nitrosation in *anhydrous* methanolic hydrogen chloride with sodium nitrite or nitrogen oxides. However, 4-nitrosodiphenylamine is unpleasant to handle. A related procedure nitrosates phenol (predominantly para), etherifies, and finally displaces the alkoxyl group with aniline.[2] The overall yield is lower, and etherifying the nitrosophenol before anilinolysis is inconvenient and expensive.

Another important synthesis involves condensation of aniline or an acylanilide with *p*-nitrochlorobenzene to 4-nitrodiphenylamine (or its *N*-acyl derivative). The condensation usually requires some form of copper and a base to neutralize

the hydrogen chloride by-product. The classical Goldberg procedure[3] heats aniline with *p*-nitrochlorobenzene, 10–20 mol % of cuprous iodide (or copper metal and potassium iodide), and a slight excess of *potassium* carbonate. Sodium carbonate, for unexplained reasons, gives much poorer results.

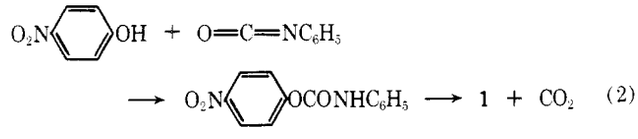


(1)

1

Goldberg showed that reaction is faster with acetanilide than with aniline, and applied the synthesis also to unactivated aryl halides.[4] Ullmann and Dahmen increased the reactivity of *p*-nitrochlorobenzene by sulfonating it,[5] but the extra steps disqualify their procedure for commercial use. Many patents over the years claim to improve the Goldberg procedure through use of formanilide, different forms of copper and various bases, and by addition of dimethylformamide.[6] With formanilide, the presumed intermediate *N*-formyldiarylamine decarbonylates during the reaction so that subsequent hydrolysis is not required.

Miscellaneous methods include dimerization of nitrosobenzene in concentrated sulfuric acid to 4-nitrosodiphenylhydroxylamine;[7] more recently trifluoroacetic acid,[8] anhydrous hydrogen fluoride,[9] and 85% sulfuric acid[10] have given better yields. However, no commercially attractive synthesis of nitrosobenzene exists, despite a good try by Dodman's group.[11] Blabak[12] ingeniously coupled *p*-nitrophenol with aniline in 72–84% yield by heating the phenol with phenyl isocyanate and a little base.



(2)

Small amounts of 4-aminodiphenylamine have been reported as by-products in other reactions. Thus it is detected when phenylhydroxylamine is rearranged to *p*-aminophenol in hot acid.[13]

p-Nitrophenylation of formanilide was selected for detailed evaluation as a commercial synthesis. Simultaneously (section II), azo coupling with diphenylamine was explored.

Discussion

I. Condensation of Sodium Formanilide with *p*-Nitrochlorobenzene. The condensation of PNCB with aniline is very slow in the absence of copper; in the absence of an added base stronger than aniline, even that slow reaction soon stops. Apparently *anilide* ion $C_6H_5NH^-$ is the active nucleophile, yet its concentration is too low to permit a rapid bimolecular reaction with PNCB. Use of a copper promoter was rejected a priori since it would have to be recovered to avoid pollution problems. Formanilide and other acylanilides are stronger acids than aniline, hence the equilibrium concentration of anion $C_6H_5N(CHO)^-$ is higher; the condensation reaction is considerably faster with formanilide than with aniline, even without copper. Logically, the equilibrium concentration of reactive anion could be increased further by using a base stronger than the expensive potassium carbonate. This hypothesis was quickly verified by showing that sodium anilide (C_6H_5NHNa) reacted very rapidly—and uncontrollably—with PNCB. Attention was thus diverted to the sodium salt of formanilide prepared from formanilide and sodium hydride. Its solution or slurry reacted with PNCB in about one-third the time required when potassium carbonate was the base. Sodium hydride is rather expensive for commercial use, however.

Formanilide reacts with sodium metal in boiling toluene with the speed of a titration, so the exothermic "neutralization" is easy to control by adjusting the formanilide addition rate. The resulting suspension of sodium formanilide then reacts with PNCB quite rapidly. Addition of dimethylformamide (DMF) brought the salt into solution and permitted complete reaction in about 2 h at 150–160 °C; yields of 1 were 87–91%.

Attempts to prepare sodium formanilide by reaction of formanilide with sodium in DMF (instead of toluene) gave much lower yields of poor quality 1. Side reactions of sodium with DMF are blamed for this.[14,15] Evidently hydride ion added to DMF to yield a powerful reducing agent.

Condensation of sodium formanilide with PNCB should yield *N*-phenyl-*N*-*p*-nitrophenylformanilide. This was synthesized independently by formylating 1 with formic–acetic anhydride, and it proved to be reasonably stable under the reaction conditions. Yet it was never detected (GC) in the crude condensation product. Instead, carbon monoxide (and some carbon dioxide) are evolved during the condensation. Evidently the carbon monoxide is lost at the same time as chloride ion leaves the cyclohexadienone intermediate.

The following procedure is nearly optimum in terms of yield, product quality, speed of operation, and recovery of solvents. Sodium (1.1 g-atoms) is melted under toluene and 1.2 mol of formanilide is added rapidly. PNCB (1.0 mol) and DMF are added and the toluene is distilled out. After 2 h at 150–160 °C, the solvents are removed and the crude residue is washed free of salts. This crude product is satisfactory for reduction to 4-aminodiphenylamine, although recrystallized material naturally was reduced more rapidly.

By-Products. Further arylation of 1 yielded 4,4′-dinitrotriphenylamine. Its amount could be held below 1% by using 10–20% excess of formanilide.

Other by-products were separated by washing the crude product with methanol and processed further by distillation, crystallization, and GC/MS. The chief component of the methanol-soluble fraction was 4-chloroazobenzene; minor components were 4,4′-dichloroazobenzene and its azoxy relative. These are obviously derived by a reduction, most likely caused by the formyl group of formanilide or diphenylformamidine. Carbon dioxide was indeed found in the off-gases from the condensation. Small amounts of diphenylurea and 4-chlorodiphenylurea were also isolated. Several compounds identified provisionally by GC/MS were a phenylbenzimidazole (mass 194), a chlorophenazine (214.5), an isomer of nitrodiphenylamine, possibly an aminonitrobiphenyl (214), and a phenylchlorobenzimidazole (228.5).

Reasonable mechanisms for the azo, azoxy, and urea compounds can be written in terms of addition of formanilide anion or diphenylformamidine anion to the nitro group, followed by internal oxygen transfer and eventual decarboxylation. The other products doubtless arise from nucleophilic substitution ortho to the nitro group.

Other Nitrodiphenylamines and Related Reactions. Various substituted formanilides were condensed under the conditions described above with substituted ortho/para nitrohalobenzenes. The results are collected in Table I. Clearly formanilides are superior to acetanilides or benzanilide. The reaction may be limited to *N*-aryl amides, since *N*-cyclohexylformamide gave poor results and valerolactam yielded mostly tar. Milder conditions might have given higher yields with the reactive *o*-nitrochlorobenzene.[16] Acetanilide, when added slowly to molten sodium, gave a sudden vigorous reaction, perhaps a Claisen condensation. However, inverse

Table I. Nitrodiphenylamines[a]

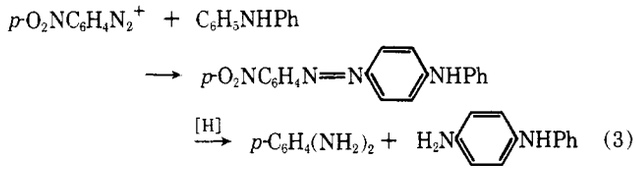
No.	Amide	Registry no.	Halide	Registry no.	Product (yield, %)	Registry no.
1	PhNHCHO	103-70-8	$ClC_6H_4NO_2$-2	88-73-3	$PhNHC_6H_4NO_2$-2 (44)[b]	119-75-5
2	PhNHCHO		$ClC_6H_3NO_2$-2-CH_3-4	89-60-1	$PhNHC_6H_3NO_2$-2-CH_3-4 (low convn)[c]	16588-32-2
3	$PhNHCOCH_3$	103-84-4	$FC_6H_4NO_2$-4	350-46-9	$PhNHC_6H_4NO_2$-4 (15)	
4	$PhNHCOC_6H_5$	93-98-1	$ClC_6H_4NO_2$-2		None isolated[d]	
5	2-$CH_3C_6H_4NHCHO$	94-69-9	$FC_6H_4NO_2$-4		2-$CH_3C_6H_4NHC_6H_4NO_2$-4 (77)[e]	726-10-3
6	2-$CH_3C_6H_4NHCHO$		$ClC_6H_4NO_2$-4-Cl-2	99-54-7	2-$CH_3C_6H_4NHC_6H_3NO_2$-4-Cl-2 (85)[f]	61587-15-3
7	2-$CH_3C_6H_4NHCO$-CH_3	120-66-1	$ClC_6H_4NO_2$-4		Tar; strong exotherm	
8	4-$EtOC_6H_4NHCHO$	61587-14-2	$ClC_6H_3NO_2$-4-CF_3-3	118-83-2	4-$EtOC_6H_4NHC_6H_3NO_2$-4-CF_3-3 (69)[g]	61587-16-4
9	4-$EtOC_6H_4NHCHO$		$FC_6H_3(NO_2)_2$-2,4	70-34-8	4-$EtOC_6H_4NHC_6H_3(NO_2)_2$-2,4 (76)[h]	6943-24-4
10	4-$EtOC_6H_4NHCHO$		$ClC_6H_3NO_2$-CH_3-4		4-$EtOC_6H_4NHC_6H_3NO_2$-2-CH_3-4 (35)[i]	61587-17-5
11	$C_6H_{11}NHCHO$	766-93-8	$ClC_6H_3NO_2$-4-CF_3-3		$C_6H_{11}NHC_6H_3NO_2$-4-CF_3-3 (low; mixture)[j]	61587-18-6
12	$NH(CH_2)_4CO$	675-20-7	$ClC_6H_3NO_2$-4-Cl-2		Mostly tar	

[a] Each experiment was run once by the general procedure in the Experimental Section. [b] Mp 73–75 °C. F. Ullmann, *Ber.*, **41**, 1872 (1908), reported mp 75 °C. [c] A great deal of starting halide was recovered. [d] No nitrodiphenylamine could be recovered from the high-melting product. [e] Mp 114.5–116.5 °C. H. J. Backer and S. K. Wadman, *Recl. Trav. Chim. Pays-Bas*, **68**, 602 (1949), reported 115–116 °C. [f] Mp 97–98 °C. Anal. Calcd for $C_{13}H_{11}ClN_2O_2$: C, 59.4; H, 4.2; N, 10.7. Found: C, 60.1; H, 4.1; N, 11.0. [g] Mp 110–114 °C. Anal. Calcd for $C_{15}H_{13}F_3N_2O_3$: C, 55.2; H, 4.0; N, 8.6. Found: C, 54.3; H, 3.7; N, 8.7. [h] Mp 118–121 °C (from toluene). N. M. Cullinane, O. E. Embrey, and D. R. Davis, *J. Chem. Soc.*, 2363 (1932), gave mp 121–122 °C, but they recrystallized from alcohol. [i] Distilled (Kugelrohr) and recrystallized from benzene, mp 79–85 °C. Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.1; H, 5.9; N, 10.3. Found: C, 65.5; H, 6.1; N, 10.6. [j] Fractionally distilled (Kugelrohr). The methanol solution of the middle fraction was allowed to evaporate slowly, giving large square prisms in a matrix of needles and gummy material. The prisms were recrystallized from methanol, mp 101–103 °C. Anal. Calcd for $C_{13}H_{15}F_3N_2O_2$: C, 54.2; H, 5.2; N, 9.7. Found: C, 54.2; H, 4.9; N, 9.9. The third distillation cut was triturated with a little cold tetrahydrofuran and crystallized from methanol, mp 133–137 °C. Anal. Found: C, 42.3; H, 1.3; N, 7.2, in fair agreement with 4,4′-dinitro-3,3′-bis(trifluoromethyl)biphenyl ($C_{14}H_6F_6N_2O_4$: C, 44.2; H, 1.6; N, 7.4) (registry no., 363-95-1). The yields of both compounds were low.

addition of sodium to a hot solution of acetanilide in toluene yielded a usable slurry of sodium salt (and by-products?). With benzanilide, only high-melting materials were obtained, but no nitrodiphenylamine.

The condensation of sodium *N*-arylformamides (ex sodium metal) and activated aryl halides appears to be reasonably general. Each pair of reactants will require some study for optimization.

II. Azo Coupling to Diphenylamine, Then Hydrogenation. Azo coupling with an active diazonium salt, followed by reductive cleavage (as with sodium dithionite), is a standard method for introducing an amino group para to an electron-releasing aromatic substituent.[17] Since diphenylamine is inexpensively available by pyrolysis of aniline hydrochloride, this method was investigated concurrently with the condensation route described above. From *p*-nitrobenzenediazonium ion as the coupling component, the coproduct is the valuable *p*-phenylenediamine.



Diphenylamine is insoluble in water, so that organic solvents have been used to achieve reasonable coupling.[17b] More basic aromatic amines will couple in dilute acid solution, but the acid may not be strong because coupling occurs with the unprotonated amine in equilibrium with the coupling-inactive anilinium salt. Use of an organic solvent meant economic death for this route. One possible alternative was coupling in warm aqueous hydrochloric acid (diphenylamine melts at 53 °C) with an emulsifying agent. Coupling with *p*-sulfo- or *p*-nitrobenzenediazonium ion under these conditions required many hours for completion. I therefore sought an aqueous sulfuric acid medium in which coupling might be more rapid.

Solubility tests showed that diphenylamine was at least 1% soluble (w/v) in 30–35% sulfuric acid, but less soluble below 25% or above 40%. If coupling were to be conducted in strong acid, the monoazo dye would be somewhat soluble and susceptible to a second coupling in the other ring. Although the dye was not soluble to the extent of 1% in 10–70% sulfuric acid, the color of the solution was much more intense above 40% concentration. With this background, *p*-nitroaniline was diazotized in nitrosylsulfuric acid (18 or 28% in 70–75% sulfuric acid) at 28–35 °C. Diphenylamine was added and the acid strength was adjusted to 25–30%. Coupling was very rapid, and the mixture soon became unstirrable. A number of detergents and wetting agents were tested to improve stirrability; 1-octanol proved to be highly effective. Coupling was complete in 15–30 min at ambient temperature.[18]

The dye was purified by washing with water, and the dried material was boiled with heptane to remove unchanged diphenylamine. The dye was accompanied by a little disazo compound (?) which was insoluble in hot benzene. Selected experiments are presented in Table II.

It is obvious that conversions are best in 25–30% sulfuric acid and that less disazo compound is formed there than at higher acid concentrations. The latter effect was particularly noticeable when the diluting water was added gradually over 1 h to permit extensive coupling in the 40–60% concentration range. No significant effect of temperature on conversion, yield, or "tar make" was seen.

The dye was hydrogenated over palladium/carbon in water suspension at 150 °C, either in the crude form or after heptane or benzene treatment. Since the dry dye was very difficult to wet, a surfactant was required. However, damp crude washed dye could be hydrogenated readily. The hot product from the autoclave was filtered to remove catalyst and worked up either by fractional vacuum distillation or by partition between

Table II. Coupling of *p*-Nitrobenzenediazonium Bisulfate to Diphenylamine in Aqueous Sulfuric Acid[a]

% H_2SO_4[b]	Time, min	Temp, °C[c]	Crude dye, mp, °C	Extd dye,[d] mp, °C	Yield, %[d]	Convn, %[e]	Benzene insol, %
30	53	40–55	134–137	138–140	90	95	7.5
30	100	22	133–135	145–148	93	83	4.1
30–25[f]	30	40	143–145	146–148	98	96	
35	66	40	110–116				
35	66	50	180–185				
25[g]	30	45	146–149	148–151	100	93	
25	100	22	142–144	147–149	97	91	2.9
25	60; 30	25; 45		140–143	100	82	4.4
25	45	45	138–141	143–145	94	99	4.9
25	65	40–55	136–140	138–140	97	95	7.5

[a] Except as noted, the *p*-nitroaniline:diphenylamine (PNA:DPA) ratio was 1.06 and the nitrosylsulfuric acid concentration was 28%. [b] Sulfuric acid concentration calculated by ignoring the organic material. [c] Where two temperatures are shown, the first is the temperature on mixing, the second is the highest reached during coupling. [d] Based on unrecovered DPA; the crude dye was extracted with heptane. [e] 100 − recovered DPA. [f] PNA:DPA 1.12; 18% $NOHSO_4$. After 5 min, added water to reduce concentration to 25%. [g] 18% $NOHSO_4$.

water and benzene at 70–75 °C. Distillation was preferred because the difference in boiling points (given for atmospheric pressure) permitted separation of *p*-phenylenediamine (267 °C), diphenylamine (302 °C), *o*-aminodiphenylamine (332 °C), and *p*-aminodiphenylamine (354 °C). The proportion of ortho isomer was determined (GC) to be 2–3%. The yield of *p*-aminodiphenylamine, based on diphenylamine consumed or *p*-nitroaniline charged, exceeded 80% in most runs.

The choice between the condensation and azo coupling routes depends upon economic and engineering factors such as cost of raw materials, availability of equipment, ease of recovery of solvents or sulfuric acid, markets for coproducts, and whether the presence of ortho isomer is permissible in the final *p*-aminodiphenylamine. In the laboratory, the two routes are equally convenient and safe.

Experimental Section

I. Condensation of Sodium Formanilide with *p*-Nitrochlorobenzene. Materials. Formanilide was prepared by heating aniline with formamide or with formic acid. In early work, the product was fractionally distilled to remove aniline and diphenylformamidine. Later, crude product was used; typically it contained (GC) 7.2% aniline, 85.9% formanilide, 6.3% diphenylformamidine, and traces of other materials. The quantity of material used was calculated from its formanilide content. PNCB was good commercial material containing only barely detectable traces of isomers or other impurities. Toluene, dimethylformamide, and sodium were commercially pure.

Typical Procedure. A 1-L four-necked round-bottomed flask was fitted with a thermometer, dropping funnel, a Dean-Stark moisture trap with its condenser connected through an oil-filled bubbler to a *trapped* wet-test meter, and a motor stirrer with a *glass* blade (sodium attacks Teflon fluorocarbon resin).[19] The flask was charged with 350 mL of toluene which was refluxed vigorously through the apparatus to remove moisture via the Dean-Stark trap, and finally 50 mL of toluene was distilled out. The flask was cooled slightly, and with a gentle nitrogen sweep, 38.0 g (1.65 g-atom) of sodium was added in large chunks. Meanwhile, 220 g (1.82 mol) of molten formanilide was added to the dropping funnel.[20] With the pot temperature above 100 °C (it is *essential* to operate above the melting point of sodium, 97.5 °C), the formanilide was added rapidly dropwise. The only limit on the rate of addition was the ability of the gas-handling system to manage the escaping hydrogen; *wide-bore* connections are required. The heat of reaction was taken up by the refluxing toluene. Stopping the addition stopped the gas evolution immediately. Typically, 15–20 min was required for formanilide addition. With a gas-tight system, over 90% of the theoretical hydrogen was measured. *Hazard:* flammable hydrogen must be vented safely.

With a nitrogen sweep, 236.0 g (1.50 mol) of PNCB was added to the slurry in one portion. Then 100 mL of DMF was added slowly while toluene was distilled out. A modest fractionating column may be used advantageously. The DMF may also be added all at once with the PNCB. A red color developed and the solids dissolved. As the toluene was removed, the temperature rose, and at about 150–155 °C a mild exotherm ensued as gas evolution began. The exotherm was readily controlled by dropping the heating mantle briefly; external cooling was rarely needed. When the exotherm was spent, the material was held at the desired temperature, usually 150–165 °C, for 2 h. The reaction was monitored by gas evolution and by GC analysis for unchanged PNCB. Usually 0.6–0.8 mol of gas per mole of PNCB was obtained. Infrared analysis showed that 10–20% of the gas was carbon dioxide, the rest carbon monoxide.

The apparatus was fitted with a head for vacuum distillation, and the pressure was gradually reduced to 10 mm, pot temperature to 150–165 °C, to remove solvents. The vacuum was broken with nitrogen, and 90 mL of 30% sodium hydroxide solution was added dropwise to the hot residue to begin the hydrolysis of excess formanilide. The mixture was steam distilled until 2 L was collected; aniline and residual PNCB were thus removed. The pot contents were cooled slowly to about 80 °C to induce the product to solidify in small granules, then chilled rapidly to 25 °C.

The solid was collected and washed with water. Since the granules trapped salts and caustic, it was necessary to wash several times in a blender until the wash water was neutral. The dried product was analyzed by melting point and by GC on a 5 ft × 0.25 in. stainless steel column packed with 3% "Silar 5CP", temperature program 150–275 °C at 21 °C/min. "Tar" was the residue from sublimation at 200 °C (0.1 mm). The yield, 85–94% on the 1.5-mol scale, was calculated from the weight of dry product after deducting "tar." The major part of the tar was 4,4′-dinitrotriphenylamine which was isolated and compared with authentic material. GC showed 0.7–4.0% of this material, depending on the amount of formanilide used.

The procedure was run three times in 10-gal equipment with 60 mol of PNCB, giving 87–91% yields. Stringent safety precautions are required with this quantity of sodium metal.

4,4′-Dinitrotriphenylamine was prepared by converting 4-nitrodiphenylamine to its salt with sodium hydride in diglyme at 100 °C. The dark red suspension was mixed with 10% excess PNCB and heated for 1.5 h at 160 °C. The excess halide was removed by steam distillation, and the solid was fractionally crystallized from 80% acetic acid, following Bugai.[21] Although large losses were encountered, product melting at 193.0–193.5 °C was obtained which, after sublimation at 220 °C (0.02 mm), melted at 194.5–195.8 °C. Mass spectrometry gave a mass number 335, confirming the assigned structure. Bugai reported mp 207 °C, but he did not characterize his product completely.

Hydrogenation of 4-Nitrodiphenylamine. A mixture of 150 g (0.70 mol) (dry basis) of washed 1, 250 mL of water, and 0.24–0.48 g of 5% Pd/C was shaken at 150 °C under 500 psig hydrogen pressure supplied via a constant-pressure valve from a calibrated reservoir. The theoretical 2.1 mol of hydrogen was absorbed in 1–2 h. Recrystallized material was reduced most rapidly, but methanol-washed and water-washed material gave satisfactory rates. *Hazard:* standard precautions must be taken for handling flammable hydrogen under pressure.

The hot product was filtered to remove catalyst. Water could be removed by distillation or by filtration of the cooled product. The 4-aminodiphenylamine could be vacuum distilled or used directly in crude form.

II. Azo Coupling of *p*-Nitrobenzenediazonium Bisulfate to Diphenylamine. Typical Procedure. Commercial nitrosylsulfuric acid, 38% $NOHSO_4$ in 86.5% sulfuric acid (thus 100 g contains 38 g of $NOHSO_4$, 53.6 g of sulfuric acid, and 8.4 g of water), was diluted with the aqueous sulfuric acid required to give 18 (or 28)% $NOHSO_4$ and 75% H_2SO_4 in a large beaker with an anchor-type glass stirrer. *p*-Nitroaniline (1.00 mol) was added fairly rapidly to 1.03–1.08 mol of this reagent while the temperature was maintained at 28–35 °C by external cooling. After 2 h, the excess reagent was destroyed with a little 15% aqueous sulfamic acid, and the solution was filtered to remove a little solid (diazoamino compound?) often present. Diphenylamine, 0.85–0.95 mol/mol of nitroaniline, preferably micropulverized, was added, followed by 5–10 mL of 1-octanol (see text). The calculated amount of water or ice (note that 1 mol of water is formed in the diazotization) was added all at once to give the desired acid strength; the heat of dilution raised the temperature 5–10 °C. Enough heat was liberated during the coupling to raise the temperature 10–20 °C during 0.5 h; the temperature can be controlled readily. The deep red dye precipitated rapidly, but the octanol permitted easy stirring. After 30–100 min, the dye was collected on a sintered-glass filter; alternatively, the mixture could be first diluted with more water. The dye was washed acid free and dried at 100 °C for analysis.

An aliquot was boiled with heptane (3–5 mL/g), cooled, and filtered. The solubilities at 25 °C follow: diphenylamine, 7.64; dye, 0.09 g/100 mL. The filtrate was evaporated on a rotary evaporator to determine the unchanged diphenylamine. The insoluble dye was boiled with benzene or toluene (10–15 mL/g), and the hot mixture was filtered through a heated, tared funnel which was then washed with hot solvent. The dark red, insoluble material melted above 250 °C; it was not further characterized, though it was believed to be the disazodiphenylamine. The dye crystallized as the filtrate cooled. Pure material melted at 157.5–158.0 °C (lit. 151[17] or 152–153 °C[22]).

Anal. Calcd for $C_{18}H_{14}N_4O_2$: C, 67.9; H, 4.4; N, 17.6. Found: C, 67.4; H, 4.3; N, 17.2.

Hydrogenation. The crude, wet, acid-free filter cake was reduced in water in an autoclave at 150 °C, 500 psig hydrogen, over 5% Pd/C. Materials with low "tar" content were reduced most rapidly. The autoclave was vented at 80 °C, and the hot liquid was filtered rapidly on a heated funnel *under nitrogen;* a pressure filter worked best. The filtrate was then fractionated at reduced pressure to separate the water, *p*-phenylenediamine, diphenylamine, and aminodiphenylamines. The ortho and para isomers can be separated with an efficient column. GC analysis (5 ft × 0.25 in. stainless steel column, 20% SE-30 on Chromosorb W AW-DMCS) showed that only 2.5–3.0% of ortho isomer accompanied the para compound. The yields of *p*-phenylenediamine and aminodiphenylamine were each over 85% based on the amount of monoazodiphenylamine present in the crude filter cake.

Acknowledgment. I am indebted to Dr. James Kalil for bringing to my attention the need for an improved synthesis of 4-aminodiphenylamine, and for his suggestion that the copper salt could be omitted from the Goldberg synthesis. Mr. Edward A. Christy provided technical assistance.

Registry No.—**1**, 836-30-6; sodium formanilide, 613-99-0; *p*-nitrochlorobenzene, 100-00-5; 4,4′-dinitrotriphenylamine, 1100-10-3; *p*-nitrobenzenediazonium bisulfate, 32968-01-7; diphenylamine, 122-39-4; 4-aminodiphenylamine, 101-54-2; 4-(4-nitrobenzeneazo)diphenylamine, 2581-69-3; 2-aminodiphenylamine, 534-85-0; *p*-phenylenediamine, 106-50-3.

References and Notes

(1) N. V. Martynov, I. T. Vaydanich, L. V. Muratova, and V. S. Tlimakhova, *Khim. Prom. (Moscow)*, 24–27 (1972).
(2) J. T. Hays, E. H. de Butts, and H. L. Young, *J. Org. Chem.*, **32**, 153 (1967); J. T. Hays, H. L. Young, and H. H. Espy, *ibid.*, **32**, 158 (1967). See also numerous related U.S. Patents.
(3) I. Goldberg, German Patent 185 663.
(4) I. Goldberg, *Ber.*, **40**, 4541 (1907).
(5) F. Ullmann and R. Dahmen, *Ber.*, **41**, 3746 (1908).
(6) A few of the numerous patents are listed: German Patent 1 056 619; French Patent 1 094 452; Japanese Patent 71 09452R; U.S. Patents 2 742 350, 2 927 943, 3 053 986, 3 055 940, 3 065 269, 3 121 736, 3 155 727, 3 277 175, 3 313 854, 3 435 074.
(7) E. Bamberger, H. Büsdorf, and H. Sand, *Ber.*, **31**, 1513 (1898); E. Bamberger and W. Ham, *Justus Liebigs Ann. Chem.*, **382**, 82 (1911).
(8) J. H. Boyer and S. E. Ellzey, *J. Org. Chem.*, **24**, 2038 (1959).
(9) U.S. Patent 3 142 705.
(10) British Patent 1 257 984. See also British Patents 1 296 211 and 1 304 525.
(11) U.S. Patent 3 578 720; British Patents 1 203 698, 1 251 836, 1 251 844.
(12) U.S. Patent 3 847 990.
(13) E. Bamberger and J. Lagutt, *Ber.*, **31**, 1506 (1898).
(14) H. Bredereck, F. Effenberger, and R. Gleiter, *Angew. Chem.*, **77**, 964 (1965); L. L. Contois, U.S. Patent 2 817 649.
(15) Other dipolar aprotic solvents were tested. Hexamethylphosphoramide gave equivalent results, but its newly discovered carcinogenic properties made it unattractive. Dimethylacetamide gave equivalent speed, but the product was lower melting, perhaps because of Claisen condensations. Dimethyl sulfoxide gave very fast reactions, but the crude product, even after extensive washing, could never be hydrogenated. Since DMF is the least expensive of the usable solvents, no detailed study was made of the others.
(16) *o*-Nitrodiphenylamines are readily cyclized to phenazine derivatives by heating with base, as in the well-known Wohl–Aue reaction. See, for example, I. J. Pachter and M. C. Kloetzel, *J. Am. Chem. Soc.*, **73**, 4958 (1951); **74**, 971 (1952); S. B. Serebryanyi, *Ukr. Khim. Zh.*, **21**, 350 (1955); *Chem. Abstr.*, **49**, 14773 (1955).
(17) (a) R. Schröter in Houben-Weyl, "Methoden der Organischen Chemie", Vol. 11, 4th ed, E. Müller, Ed., Georg Thieme Verlag, Stuttgart, 1957, Chapter 4, p 522; (b) British Patent 770 299; A. Meldola, *J. Chem. Soc.*, **43**, 440 (1883).
(18) The familiar spot tests on filter paper can be used to follow the coupling when the diazonium salt is not in excess. With an excess, the conversion of diphenylamine did not increase significantly after about 15 min.
(19) The stirrer bearing must resist boiling toluene and also be vacuum tight for the subsequent distillation. A Chesapeake seal proved best, but it required frequent O-ring replacement. A well-lubricated *new* Trubore bearing could also be used.
(20) Molten formanilide readily supercools, and it did not require heating to keep it molten. A "heat gun" was kept available.
(21) P. M. Bugai, *J. Gen. Chem. USSR (Engl. Transl.)*, **23**, 627 (1953). See also R. Herz, *Ber.*, **23**, 2536 (1890).
(22) N. Voroshov, *Zh. Obshch. Khim.*, **47**, 1732 (1916); *Chem. Zentralbl.*, Ser. II, 261 (1916).