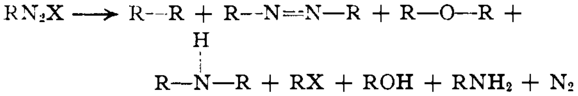
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF NEW HAMPSHIRE]

Symmetrical Biaryls from Diazotized Amines. Scope of the Reaction. Unsymmetrical Biaryls

BY EDWARD R. ATKINSON, C. R. MORGAN, H. H. WARREN AND T. J. MANNING

The first paper in this series[1] outlined an extensive study of the reduction of diazotized amines in aqueous solution which proceeds according to the generalized equation



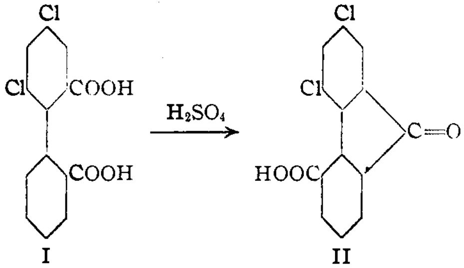
$$RN_2X \longrightarrow R{-}R + R{-}N{=}N{-}R + R{-}O{-}R + R{-}\overset{\displaystyle H}{\overset{|}{N}}{-}R + RX + ROH + RNH_2 + N_2$$

Later papers[2] described investigations of a variety of reducing agents and experimental conditions used in the reaction. The present paper describes the reduction of a number of diazotized amines and in addition reports the first synthesis of an unsymmetrical biaryl by this method.

The only previous attempt to determine the scope of this reaction was that of Vorländer and Meyer.[3] Their work undoubtedly inspired all subsequent use of this reaction but they unfortunately employed a number of reducing agents, and in many cases failed to state which one of these was used in the reduction of a particular diazotized amine. Furthermore the method of adding the diazo solution to the reducing agent was not considered to be a critical factor by them, while we have found that the use of the addition tube described by us[1] is necessary in most cases.

In the present work we have used a single reducing agent (cupro-ammonia ion in dilute ammonium hydroxide, prepared by reducing ammoniacal copper sulfate solutions with hydroxylamine) and a set of experimental conditions which in our earlier work[2] gave excellent results. The results of our study are summarized in the table. We have included certain results obtained previously in this and other laboratories; these results are comparable with those of the present work because the reducing agent and the experimental conditions used were either identical with those employed in the present work or were a reasonable equivalent of them. The only products examined were those which were essentially insoluble in water and the yields reported in most cases represent minimum yields since there were unavoidable losses in purification.

The possibility of synthesizing unsymmetrical biaryls by the reduction of a mixture of diazotized amines was suggested in our first paper.[1] When mixtures of diazotized *o*-nitroaniline and diazotized anthranilic acid were reduced under our "standard" conditions we obtained products which were identical with those obtained when the substances were reduced separately; similar results were obtained with a mixture of diazotized *p*-nitroaniline and diazotized anthranilic acid. However, when a mixture of diazotized anthranilic acid and diazotized 3,5-dichloro-2-amino-benzoic acid was reduced the new 4,6-dichlorodiphenic acid (I) was formed in 15–20% yields along with the usual symmetrical products. Treatment with concentrated sulfuric acid converted this substance to 2,4-dichlorofluorenone-5-carboxylic acid (II).



I II

Since the separation of the unsymmetrical product was difficult we did not study the effect of various factors on its yield. The formation of the unsymmetrical biaryl is of particular interest in connection with a study of the reaction mechanism; such a study is now in progress in this Laboratory.

Experimental Part

All melting points reported in this paper were observed by use of a copper block equipped with a small magnifying lens. A 360° rod form melting point thermometer was used. All melting points are uncorrected.

General Experimental Procedure.—All amines were Eastman Kodak Co. materials which were recrystallized or distilled until they possessed melting or boiling points given in the literature. Diazotization was by the direct method unless otherwise stated. Hydrochloric acid was used exclusively. All diazo solutions were protected from excessive illumination and were filtered before use. None were discolored.

Ten-gram or 20-g. samples of the amines were used. The preparation of the cupro-ammonia reducing solution and the technique for its use have already been described.[12] The mole ratio Cu^+/RN_2X, the concentration of the various ingredients in the reducing solution, and all other experimental conditions were similar to those previously used for anthranilic acid.[12,13] It has already been shown[2a] that minor variations in mole ratios and concentrations have little if any effect on the course of the reaction.

Non-acidic products appeared as a precipitate or oil during the reaction. These were filtered or extracted from the ammoniacal solution. Acidic products were isolated by acidification of the reaction mixture. The filtrates contained the more soluble products (RX, etc.) and no attempt was made to isolate these quantitatively. Analytical methods for the water insoluble products involved no unusual procedures. Separation of products in some cases was difficult; however, stated yields are those actually isolated.

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(1) Atkinson and Lawler, THIS JOURNAL, **62**, 1704 (1940).

(2) (a) Atkinson, *et al.*, *ibid.*, **63**, 730 (1941); (b) **65**, 476 (1943).

(3) Vorländer and Meyer, *Ann.*, **320**, 122–144 (1902).

TABLE I

PRODUCTS FROM THE REDUCTION OF DIAZOTIZED AMINES

RN_2Cl from	R—R	RN=NR		Other products isolated
	Yield, %	Yield, %	M. p., °C.	
Aniline	Small[a]	45	67– 68	ROH
o-Toluidine	None	45	53– 54	ROH, RCl[b]
m-Toluidine	None	27	50– 52	ROH[c]
p-Toluidine	None	50	140–142	ROH,[d] RCl[e]
o-Nitroaniline	45[f]	3	217–218	RCl (14%), m. p. 30–32°
m-Nitroaniline	45[g]	3	150–153	RCl (13%), m. p. 43–44°
p-Nitroaniline[h]	12[i]	Small[j]	220–222	RCl (14%), m. p. 81–82°[k]
2-Methyl-6-nitroaniline[4]	24	16		
2-Methyl-4-nitroaniline[5]	31			
2-Nitro-4-methoxyaniline[4]	64	Small		
p-Aminophenol	None	45	212–216 dec.	
p-Aminoacetanilide	None	28	287–290 dec.	
Anthranilic acid[12,13]	85–90	None		RNHR
2-Aminobenzoic acid derivs.				
4-chloro[6,7]	75	None		RX, ROR, ROH
5-chloro[8]	50	None		RX, ROH
6-chloro[7]	80	None		
3,5-dichloro[m]	50	None		RCl, RNH_2
3,5-dibromo[1]	40	None		RCl, RNH_2
4-nitro[9]	61			
6-nitro[10]	40			RCl
m-Aminobenzoic acid	None	31[n]	340 dec.[16]	RCl
p-Aminobenzoic acid	None	35[n]	350 dec.[16]	
o-Aminobenzenesulfonic acid[o]	20			
Aminonaphthalene carboxylic acids[11,p]	High			

[a] Qualitative test. [b] Derivative: *o*-chlorobenzoic acid, m. p. 136–139°. [c] Derivative: 2,4,6-tribromo-3-methylphenol, m. p. 80–82°. [d] Derivative: 2,6-dibromo-4-methylphenol, m. p. 47–49°. [e] Derivative: *p*-chlorobenzoic acid, m. p. 234–236°. [f] M. p. 120–122°. [g] M. p. 190–196°. Recrystallization from acetone gave 27% yield, m. p. 203–205°. [h] Reduction complete only if reaction carried out at 30–35°; after removal of RCl, 4 g. of residue was alkali-soluble tar, 3 g. a mixture of R—R, R—N=N—R, RNHR, which could not be quantitatively separated. [i] M. p. 233–235°. [j] Separated mechanically from a sublimate. [k] Also RNHR by qualitative color test by addition of alkali to acetone solution.[14] Color discharged by hydrosulfite, reduction passing through green intermediate stage. [l] The red-brown beta form.[15] [m] Present procedure preferable to that previously described by us.[1] Runs employing as much as 50 g. of amine have been carried out. [n] From butyl carbitol. [o] See Experimental part. [p] Used commercially in preparation of anthanthrone dyestuffs.

At least two runs were carried out with each amine and the results given in the table are those for a typical run.

***o*-Aminobenzenesulfonic Acid.**—To prevent separation of the diazo salt the diazo solution was diluted to 300 cc. The reaction mixture was boiled down to 100 cc., acidified with sulfuric acid and copper eliminated as the sulfide. A number of unsuccessful attempts were made to isolate homogeneous fractions of the barium and sodium salts by the conventional procedures. In a typical run all products were isolated as the sodium salts and the latter (42 g.) were heated for two hours with 70 g. of phosphorus pentachloride and the resulting sulfonyl chlorides isolated in the usual way. Two grams (20% yield) of the acid chloride of biphenyl-2,2′-disulfonic acid, m. p. 139–140°,[17] was obtained after recrystallization from chloroform. It was further identified by conversion to the anilide,[17b] m. p. 165–166°. The aqueous solutions of the salts were brown in color. This color was discharged by alkaline hydrosulfite.

Reduction of a Mixture of Diazotized Amines.—Ten grams (0.048 mole) of pure 3,5-dichloro-2-aminobenzoic acid, m.p. 227–229°, was diazotized exactly as previously described.[1] Ten grams (0.072 mole) of anthranilic acid was diazotized as for the preparation of diphenic acid.[2a,13] The reducing solution was simply a combination of the solutions prepared as usual for the individual amines; amounts of materials were approximately twice those used for 10-g. samples of anthranilic acid alone.

The reaction was carried out in the usual way after mixing the two diazo solutions. The crude was precipitated by careful acidification of the reaction mixture. It was dissolved and reprecipitated from dilute bicarbonate solution and then weighed about 14 g., m. p. 170–200°. The crude was subjected to diazotization to remove 3,5-dichloro-2-aminobenzoic acid which is known to be a by-product.[1] It then weighed 11.3 g. It was leached three times with 100-cc. portions of boiling water. The water-soluble material proved to consist chiefly of diphenic acid. The water-insoluble residue (6.3 g.) was then leached twice with 100-cc. portions of benzene. The residue (2 g., m. p. 213–255°) was shown to consist chiefly of *d,l*-4,6,4′,6′-tetrachlorodiphenic acid by recrystallization from concentrated sulfuric acid.[1]

The benzene solution was concentrated by boiling and a total of 3.1 g. of a colorless solid, m. p. 212–216°, obtained.

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(4) Lothrop, THIS JOURNAL, **64**, 1698 (1942).

(5) Sherwood and Calvin, *ibid.*, **64**, 1351 (1942).

(6) Hunn, *ibid.*, **45**, 1024 (1923).

(7) Huntress and Cliff, *ibid.*, **55**, 2559 (1933).

(8) Huntress, Cliff and Atkinson, *ibid.*, **55**, 4262 (1933).

(9) Case and Koft, *ibid.*, **63**, 509 (1941).

(10) Atkinson, Ph.D. Thesis, Mass. Inst. of Tech., 1936, pp. 146–158.

(11) German Patent 445,390: *Friedländer*, **15**, 300 (1928).

(12) Ref. 2a, Method 2.

(13) Atkinson and Lawler, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 222.

(14) Hantzsch, Hein and Hardtmann, *Ber.*, **52**, 498 (1919).

(15) Willstätter and Benz, *Ber.*, **39**, 3500 (1906).

(16) Carré, *Compt. rend.*, **141**, 595 (1905).

(17) (a) Barber and Smiles, *J. Chem. Soc.*, 1145 (1928); (b) Limpricht, *Ann.*, **261**, 329 (1891).

By recrystallization twice from ethyl acetate–ligroin there was obtained one-half gram of 4,6-dichlorodiphenic acid (I) white needles, m. p. 216–217°.

Anal. Calcd. for $C_{14}H_8O_4Cl_2$: Cl, 22.8; neut. equiv., 155.5. Found: Cl, 23.0; neut. equiv., 154.

Because of the difficulties in isolating this material the quantitative determination of its formation was carried out by treatment of the original crude with concentrated sulfuric acid (see below).

A number of experiments were performed in which mixtures of diazotized anthranilic acid and diazotized *o*- or *p*-nitroanilines were reduced. The only acidic product was pure diphenic acid.

2,4-Dichlorofluorenone-5-carboxylic Acid (II).—Three-tenths gram of 4,6-dichlorodiphenic acid was heated with 2 cc. of concentrated sulfuric acid for ten minutes at 150° or for two days at 80°. The resulting solution was poured on ice and the yellow solid dissolved in warm dilute bicarbonate solution (in some experiments the sodium salt crystallized if the solution was cooled). After reprecipitation with dilute hydrochloric acid it was recrystallized from benzene–alcohol as yellow needles, m.p. 240–242°.

Anal. Calcd. for $C_{14}H_6O_3Cl_2$: Cl, 24.2; neut. equiv., 293. Found: Cl, 24.2, 24.3; neut. equiv., 293, 294.

The formation and isolation of this substance proved to be a convenient method for estimating the amount of 4,6-dichlorodiphenic acid when the latter was mixed with both diphenic acid and 4,6,4′,6′-tetrachlorodiphenic acid as in the crude reduction product. In a typical run 14 g. of crude was heated with 45 cc. of concentrated sulfuric acid at 150° for ten minutes or at 80° for three days. The solution was cooled and 2.6 g. (28% yield) of *d,l*-4,6,4′,6′-tetrachlorodiphenic acid filtered off. The filtrate was poured on ice and the resulting yellow solid dissolved in warm dilute bicarbonate solution and filtered free from a small amount of non-acidic material. Reprecipitation with dilute hydrochloric acid gave 6 g. of mixed fluorenone carboxylic acids. There was evidence for the presence of water soluble sulfonation products which were removed at this point. Separate experiments showed that they were derived chiefly but not entirely from the diphenic acid. The acid mixture was recrystallized from a mixture of nine parts of benzene and one part of alcohol. The first fractions were pure 2,4-dichlorofluorenone-5-carboxylic acid, m. p. 240–242°. A total of 2.5 g. melting in the range 235–241° was obtained in some runs. A separate experiment showed that when mixtures of diphenic acid and tetrachlorodiphenic acid were heated in concentrated sulfuric acid no dichlorofluorenone carboxylic acid was formed. Thus the 2.5 g. isolated above corresponds to an 18% yield of 4,6-dichlorodiphenic acid in the reduction reaction.

Summary

1. By reduction with cupro-ammonia ion in dilute ammonium hydroxide the diazotized forms of the following amines are converted to biaryls in yields of 20–90%: the nitroanilines, the nitrotoluidines, anthranilic acid, a variety of halogeno- and nitroanthranilic acids, a number of aminonaphthalene carboxylic acids, *o*-aminobenzenesulfonic acid.

2. The following yield azo compounds in yields of 20–50%: aniline, the toluidines, *p*-aminophenol, *p*-aminoacetanilide, *m*- and *p*-aminobenzoic acids.

3. Reduction of a mixture of diazotized anthranilic and 3,5-dichloro-2-aminobenzoic acids produces the unsymmetrical biaryl 4,6-dichlorodiphenic acid (I) in addition to the usual symmetrical products.

4. 4,6-Dichlorodiphenic acid is converted to 2,4-dichlorofluorenone-5-carboxylic acid (II) by heating with concentrated sulfuric acid.

DURHAM, N. H. RECEIVED JULY 14, 1945

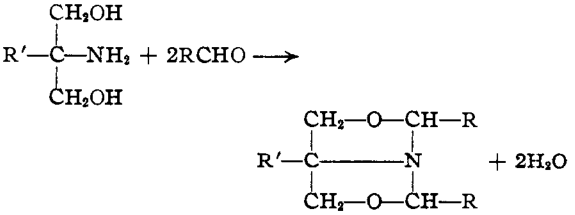
[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DEPARTMENT OF THE COMMERCIAL SOLVENTS CORP.]

Some New Derivatives of Amino Hydroxy Compounds[1]

BY MURRAY SENKUS

Amino alcohols which have an amino group or a monosubstituted amino group and an alcohol group attached to adjacent carbon atoms are known to react with aldehydes to form oxazolidines. A large number of new amino alcohols have recently become available from the hydrogenation of nitro alcohols that can be prepared by allowing one mole of a nitroparaffin to react with one mole of an aldehyde.[2] Some of these amino alcohols have been converted to oxazolidines and the new compounds are reported herein.

A study was also made of the reaction of aldehydes with amino polyhydric alcohols that can be prepared by the hydrogenation of nitro polyhydric alcohols derivable from normal nitroparaffins and formaldehyde.[2] Two types of products were obtained from the above reactions. The reaction of one mole of an aldehyde with one mole of an amino polyhydric alcohol gave an oxazolidine. The reaction of two moles of an aldehyde with one mole of an amino polyhydric alcohol gave substituted 1-aza-3,7-dioxabicyclo[3.3.0]octanes according to the scheme



The structures chosen for the new compounds are supported by analytical data and by the observation that in each reaction one mole of amino polyhydric alcohol and 2 moles of an aldehyde yielded 2 moles of water and the amount of product calculated according to the above equation.

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(1) The portion of this article describing the reactions of aldehydes with the amino polyhydric alcohols was originally received by us on September 7, 1943.—*The Editor*.

(2) Vanderbilt and Hass, *Ind. Eng. Chem.*, **32**, 34 (1940).