Chloroazobenzenes: Studies on Syntheses

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Dedicated to Prof. Dr. OTTO NEUNHOEFFER on his 65-th birthday

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Thirteen chloroazobenzenes were synthesized by reduction of chloronitrobenzenes or by oxidation of their corresponding chloroanilines. Five of the compounds have not been previously prepared or described. Reduction by LiAlH₄ was the method of choice, but it proved inadequate for the syntheses of chloroazobenzenes from o-chloronitrobenzenes. This reaction eliminated chlorine if ortho to the aniline nitrogen and an additional chlorine atom; in the other cases steric hindrance of azo bond formation resulted in low yields. Chromatographic systems for the separation of pure chloroazobenzenes from the crude reaction mixtures were developed and are described.

Results and Discussion

The synthesis of chloroazobenzenes depends in part on the starting material. Some methods are based on oxidation of the amino group of chloroanilines and others require the reduction of the nitro group of chloronitrobenzenes. EDWARD¹ oxidized primary aromatic amines to azobenzenes using benzoylperoxide (yield 5 - 20%). The oxidant used by WHEELER and GONZALES² was MnO₂ (yield 5 to 90%); and they observed that halogenoanilines substituted in the *p*-position were especially reactive in the order F>Cl>Br>I. DANIELS and SAUNDERS³ produced 4,4'-dichloroazobenzene (yield 20%) enzymatically in a system that contained *p*-chloroaniline, H₂O₂ and horseradish peroxidase in acetate buffer at pH 4.6. KREMER and BENDICH⁴ reduced chloronitrobenzenes to chloroazobenzenes (yield 40 - 80%) and other products with monoethanolamine in the presence of anhydrous Na₂CO₃, but reduction with LiAlH₄ in ether solution as described by CORBETT and HOLT⁵ proved to be a superior method for the synthesis of chloroazobenzenes (yield up to 95%). However, present results indicate that this method is not suitable for production of chloroazobenzenes from o-chloronitrobenzenes. Chlorine that was ortho to the nitro group and an additional chlorine atom, was eliminated in the course of the reaction. Chlorine ortho to the nitro group and without an adjacent chlorine atom was not eliminated, but the yield of dichloroazobenzene was low (<5%). Nitrobenzenes with chlorine substitutents in *meta* and/or *para* position produced azo compounds in yields as great as 95 per cent. These differences can be explained only by steric hindrance. Apparently, a halogen atom *ortho* to an amino or nitro group interferes sterically with the formation of an azo bond. DAINS and KENYON⁷ also noted halogen losses when substituted aromatic nitro and nitroso compounds were reduced to azoxybenzenes with sodium alcoholates. Losses amounted to as much as 62 per cent. They were not a function of the halogen but depended on the nature of the alcohol used.

Some of the reactions yielded quantities of tar, so that purification of chloroazobenzenes presented difficulties. The physical properties of chloroazobenzenes, chlorohydrazobenzenes and chloroazoxybenzenes are very similar, but they were separated by chromatography on neutral aluminum oxide (Woelm, Act. I) columns that were developed by nonpolar solvents (ligroine, benzene, toluene). Effluents were fractionated and examined by gas chromatography for di-, tetra- and hexachloroazobenzenes (DCAB, TCAB, HCAB). As a final step in the purification of all azobenzenes **, the compounds were recrystallized from acetone and their homogenity was established by thin layer and gas chromatography.

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¹ J. T. EDWARD, J. chem. Soc. [London] 1956, 222.

² O. H. WHEELER and D. GONZALEZ, Tetrahedron [London] **20**, 189 [1964].

³ D. G. H. DANIELS and B. C. SAUNDERS, J. chem. Soc. [London] **1953**, 822.

⁴ Ch. B. KREMER and A. BENDICH, J. Amer. chem. Soc. 62, 1279 [1940].

⁵ J. F. CORBETT and P. F. HOLT, J. chem. Soc. [London] **1963**, 2385.

The azobenzenes synthesized are listed in Table I. Compounds 2, 3, 4, 6, 7, 9, 10, and 12 were produced from their corresponding chloronitrobenzenes

R N=N R'		mp [°C]	Refer.
Azobenzene	(1)	68	1, 2, 9
2,2'-Dichloro-	(2)	133 - 134	5
3,3'-Dichloro-	(3)	101 - 102	5
4,4'-Dichloro-	(4)	184 - 185	1, 2, 3, 5
2,2',3,3'-Tetrachloro-	(5)	204 - 205	b, c,
2,2',4,4'-Tetrachloro-	(6)	167 - 168	1
2,2',5,5'-Tetrachloro-	(7)	190 - 191	5
2,2',6,6'-Tetrachloro-	(8)	128	b
3,3',4,4'-Tetrachloro-	(9)	158	4, 5, 8
3,3',5,5'-Tetrachloro-	(10)	193 - 194	4, 5
3,3'-Dichloro-4,4'-dimethyl-	(11)	132 - 133	b
2,2',4,4',5,5'-Hexachloro-	(12)	216 - 217	b
2,2',4,4',6,6'-Hexachloro-	(13)	193	р

Table I. Some azobenzenes ^a and their melting points ^d. ^a The UV- and IR-spectra indicated that all compounds were trans-isomers. ^b New compounds. ^c See reference 6. ^d For UV and IR characterization see reference 11.

by reduction with excess $LiAlH_4$ in ether. Since it was not possible the obtain compound 5 by this procedure, it was synthesized by mild reduction of 2,3-

	Yields obtained		Yields obtained by	
Azo- ben- zene	Reduct. of chloronitro- benzenes with $LiAlH_4$	Synthesis by other methods	Reduct. of chloronitro- benzenes with LiAlH ₄	Synthesis by other methods
1	_		_	20
2	40		40	
3	80		75 - 95	
4	80	_	75 - 95	15
5	dehalog.	5		
6	20^{-}			5
7	20		40	_
8	< 0.1	5	_	
9	80	95	75 - 95	40 - 70
10	80	_	75 - 95	40 - 60
11		75	_	—
12	5	—	-	_
13	< 1	20	—	-

Table II. Yields of azobenzenes ^a. ^a In per cent of the theoretical yields. ^b For reference see Table I.

- ⁶ H. A. B. LINKE, R. BARTHA, and D. PRAMER, Naturwissenschaften 55, 444 [1968].
- ⁷ F. B. DAINS and W. O. KENYON, J. Amer. chem. Soc. 53, 2357 [1931].
- ⁸ R. GAUDRY and K. F. KEIRSTEAD, Can. J. Research **27** B, 897 [1949].
- ** Unsubstituted azobenzene (1) was purchased from K & K Laboratories, Inc., Plainview, N. J.

dichloronitrobenzene with zinc powder in alkaline methanol⁶. Compounds **11** and **13** were produced from their corresponding chloroanilines by oxidation with MnO_2 , using the method of WHEELER and GONZALES². The oxidation of 2,6-dichloroaniline with lead tetraacetate yielded compound **8**. The chloroazobenzene yields obtained, and those reported by other authors, are summarized in Table II.

Experimental Section

Gas chromatography. A F & M Model 700 gas chromatograph with flame ionization detection aided the separation and purification of chloroazobenzenes from the crude synthetic products. Columns: 1.8 m long, 3 mm o.d. stainless steel, packed with 5% UC-W98 on Chromosorb W. Carrier: helium, 30 cc/min., oven temperature 250 °C. Retention times of azobenzenes: azobenzene 20 sec., DCAB 55-65 sec., TCAB 120 to 155 sec., and HCAB 270-310 sec.

Thin-layer chromatography for the separation of DCAB, TCAB and HCAB was performed on MN-Polygram[®] Cel 300 AC-10 sheets (Brinkman Instruments, Inc., Westbury, N. Y.) developed with glacial acetic acid:acetone (or pyridine):methanol=10:20:70 (v/v). Movement was in the order: R_f DCAB > R_f TCAB > R_f TCAB and HCAB. For the separation of DCAB from TCAB and HCAB, the preferred solvent system was H_2O : acetone:methanol = 20:20:60 (v/v) and movement was in the order: R_f DCAB > R_f HCAB. R_f HCAB. R_f HCAB > R_f HCAB. R_f HCAB > R_f HCAB.

Compounds. Activated MnO₂: 59.4 g MnCl₂·4 H₂O in 1000 ml H₂O were mixed with 31.6 g KMnO₄ in 2000 ml H₂O and the pH of the mixture was made alkaline with KOH. The precipitated MnO₂ was collected by filtration, washed with H₂O, activated at 120 °C and stored in a desiccator until used.

2,2',3,3'-Tetrachloroazobenzene (5): 15 g NaOH were dissolved in 30 ml H₂O. To this solution 10 g 2,3-dichloronitrobenzene, 100 ml methanol and 10 g zinc powder were added and the reaction mixture was refluxed for 16 hours. After cooling, it was acidified with HCl, diluted with H₂O, and partitioned with ether. The ether extract was evaporated to dryness and the residue dissolved in ligroin $(60-70\ ^{\circ}C)$ and transferred to a 30 cm chromatographic column packed with neutral aluminium oxide (Woelm, Act. I). The column was eluted with ligroin and fractions of the effluent were examined by gas chromatography for the presence of 5. Fractions containing 5 were combined, dried by evaporation and the compound was recrystal-

- ⁹ L. GATTERMANN and H. WIELAND, "Die Praxis des organischen Chemikers", p. 163, Walther de Gruyter & Co., Berlin 1956.
- ¹⁰ A. I. VOGEL, Textbook of Practical Organic Chemistry, p. 199. Longmans Green, London 1948.
- ¹¹ H. A. B. LINKE and D. PRAMER, Submitted for publication in Z. Naturforschg., Teil b.

lized from acetone. Red needles. mp: 204-205 °C. Yield: 5 per cent.

Anal. Calcd for $C_{12}H_6N_{2}Cl_4$: C 45.02; H 1.89; N 8,76; Cl 44.33. Found: C 45.09; H 1.85; N 8.91; Cl 44.23.

2,2',6,6'-Tetrachloroazobenzene (8): 5 g 2,6-dichloroaniline and 15 g freshly prepared lead tetraacetate ¹⁰ were reacted in the cold (ice bath) with stirring for 1 hour. The precipitate was collected by filtration and washed with benzene. The benzene washes were combined with the filtrate, the solution was treated with Na₂CO₃ and anhydrous Na₂SO₄ and refiltered. The benzene filtrate was evaporated to dryness, and the residue was dissolved in ligroin $(60-70\ ^\circ C)$ and purified by column chromatography as described for compound 5, with the addition of elution with benzene; the bulk of 8 was eluted by the benzene. The eluate was dried by evaporation, the residue was dissolved in toluol and rechromatographed on neutral aluminium oxide (Woelm, Act. I) column that was developed with toluol. Fractions of the eluate containing 8 were combined, evaporated to dryness and the compound was recrystallized from methanol and acetone. Green plates. mp: 128 °C. Yield: 5 per cent.

Anal. Calcd for $C_{12}H_6N_2Cl_4$: C 45.02; H 1.89; N 8.76; Cl 44.33. Found: C 45.09; H 1.84; N 8.84; Cl 44.48.

3,3'-Dichloro-4,4'-dimethylazobenzene (11): To 3.5 g 3-chloro-4-methylaniline dissolved in 150 ml benzene, 10.8 g activated MnO_2 were added. The reaction mixture was refluxed for 10 hours. The insoluble residue was collected by filtration, extracted with hot benzene, and the filtrate and washes were combined, concentrated by evaporation and compound 11 crystallized when cold acetone was added. Recrystallized from acetone. Orange needles. mp: 132–133 °C. Yield: 75 per cent. Anal. Calcd for $C_{14}H_{12}Cl_2N_2$: C 60.23; H 4.33; N 10.03; Cl 25.41. Found: C 60.53; H 4.54; N 9.27; Cl 25.38.

2,2',4,4',5,5'-Hexachloroazobenzene (12): To an icecooled solution of 12 g 2,4,5-trichloronitrobenzene in 150 ml anhydrous ether, 6 g LiAlH₄ suspended in 150 ml of cold anhydrous ether were added dropwise with constant stirring. After 2 hours at room temperature, the reaction mixture was refluxed for 15 minutes and cooled. Excess LiAlH₄ was destroyed by the dropwise addition of H₂O, and the ether phase was separated and evaporated to dryness. The residue was dissolved in ligroin (60-70 °C) and transferred to a 30 cm neutral aluminium oxide column (Woelm, Act. I). The column was developed first with ligroin and then with benzene. Gas chromatographic analysis demonstrated that the benzene eluate contained the bulk of 12. This material was evaporated to dryness and the product was recrystallized from acetone. Orange needles. mp: 216-217 °C. Yield: 5 per cent.

Anal. Calcd for $C_{12}H_4N_2Cl_6$: C 37.04; H 1.04; N 7.21; Cl 54.71. Found: C 37.13; H 1.27; N 7.61; Cl 53.41.

2,2',4,4',6,6'-Hexachloroazobenzene (13): 4.9 g 2,4,6-trichloroaniline in 150 ml benzene were refluxed for 10 hours with 10.8 g activated MnO₂. The reaction product was purified by the procedures described for compound 11 and recrystallized from an ether-acetone mixture. Red-brown needles. mp: 193 °C. Yield: 20 per cent.

Anal. Calcd for $C_{12}H_4N_2Cl_6$: C 37.04; H 1.04; N 7.20; Cl 54.72. Found: C 37.04; H 1.04; N 7.20; Cl 54.38.

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