Polychlorinated Biphenyls: Synthesis of Some Individual Chlorobiphenyls[1]

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Fundamental studies on the biological and chemical properties of polychlorinated biphenyls (PCB's) and their analytical behavior are hampered by the fact that commercial samples, such as the Aroclors, are complex mixtures of isomeric biphenyls substituted by different numbers of chlorine atoms. [For a theoretical consideration of number of isomers and the probability of their formation see (1).] Scissons and Telling, for example, have shown that Aroclor 1254 can be resolved into more than fifty components by high resolution gas chromatography employing SCOT columns (2). Since it is extremely difficult to correlate and evaluate data from such a complex mixture, we have initiated a program for the synthesis of individual chlorobiphenyls to facilitate studies on the biological and chemical properties of these compounds.

In this communication the synthesis of twenty-three chlorobiphenyls is described using a number of different synthetic routes. Three of the compounds, 2,6-dichlorobiphenyl, 2,3,4,5,6-pentachlorobiphenyl and 2,3,4,6,2',3',4',6'-octachlorobiphenyl have not previously been reported in the literature. All the above isomers were unambiguously prepared from intermediates of known structure. The most suitable method, from the point of view of availability of starting material and ease of experimental procedure, is indicated for each preparation. Although some of the chlorobiphenyls synthesized are unlikely to be present in commercial PCB mixtures these were prepared for a systematic glc and mass spectrometric study of this class of compounds.

Experimental

All chlorobiphenyls prepared were homogeneous on thin layer chromatograms (silica gel in heptane); and gave one peak when chromatographed on a 4% SE-30 column

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[(3); impurity peaks <1%]. Mass spectra, obtained for all compounds, confirmed the molecular composition (4).

Most compounds with a final m.p. below 40° were first obtained as oils which were sometimes very difficult to crystallize without seed crystals. These oils were dissolved at 25° in the solvent indicated in the Table and allowed to crystallize at temperatures between -20° and -80°.

Most suitable synthetic procedures, physical constants and R_f values in heptane for twenty-three chlorobiphenyls are reported in the Table. Details for some of the chemical procedures are given below.

Synthetic Procedures

A, Gomberg-Hey Reaction

A_1, Using sodium acetate (cf. 5) - The chloroaniline (0.1 M) was heated in concentrated hydrochloric acid (40 ml), then cooled to -5° and diazotized with a solution of sodium nitrite (10 g; 0.15 M for each amino group) in water (20 ml) at 0-5°. The mixture was stirred for 30 minutes at this temperature and then filtered, at -5°. The filtrate was added to cold, vigorously stirred benzene (500 ml) and a solution of sodium acetate $3H_2O$ (60 g) in water (150 ml) was then added portionwise with vigorous stirring. The mixture was removed from the cooling bath and stirred overnight at 25°. The benzene layer was washed with water, dried (Na_2SO_4) and evaporated to dryness. The chlorobiphenyl was purified by distillation in vacuo, recrystallization or chromatography on columns or preparative thin layer plates (see Table).

A_2, Using sodium hydroxide (cf. 6) - The reaction was carried out as under A_1 except the 5N sodium hydroxide (ca. 50 ml) was added to the cooled mixture of the diazotized chloroaniline and benzene.

B, Ullmann Reaction (7-9)

B_1, Without solvent - Equal quantities of the chloroiodobenzene derivative and copper powder (Fisher, electrolytic dust, activated by subsequent treatment with a solution of iodine in acetone and conc. HCl-acetone cf. Organic Syntheses, (Collect. Vol. 3, p. 339, note 1) were intimately mixed and heated at 220-280° for 1-4 hours with occasional stirring. The reaction mixture was cooled to 80°, TABLE

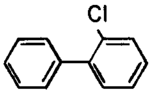
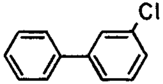
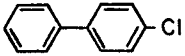
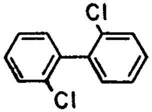
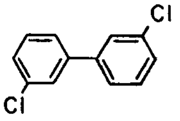
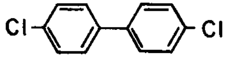
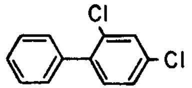
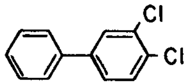
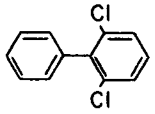
Compound[‡]		Preparation			Physical data	
					m.p.[**] °C	
Name	Formula	Starting Material (Sources[§,+])	Method[*]	Purification[‡‡]	Found Lit.	R_f[§§]×100
Monochlorobiphenyls						
2-		2-Aminobiphenyl (I)	C(13) ‡	TLC, MeOH aqu.	33-4 33.5(13)	35
3-		3-Chloroaniline (I)	A_1 (14) ‡	Dist., MeOH aqu.	16-7 Oil (14)	49
4-		-	‡	MeOH	77-8 77.7(14)	43
Dichlorobiphenyls						
2,2'-		2-Chloroiodobenzene (V)	B_1 ‡	TLC, MeOH	59-60 60.5(15)	38

TABLE (contin.)

Compound‡		Preparation			Physical data	
					m.p.**°C	
Name	Formula	Starting Material (Sources§,+)	Method*	Purification‡‡	Found Lit.	R_f§§×100
3,3'-		3,3'-Dinitrobiphenyl (II) ↓	F			
		3,3'-Diaminobiphenyl	C	TLC, EtOH aqu.	26-7 29(16)	45
4,4'-		-	‡	MeOH	148-9 148(17)	41
2,4-		2,4-Dichloroaniline (I)	A_1 (5)	TLC, MeOH aqu.	24-5 24.4(5)	50
3,4-		3,4-Dichloroaniline (III)	A_1 (5)	TLC, MeOH	45-6 48-9(5)	42
2,6-		2,6-Dichloroaniline (I)	A_1	Col., MeOH aqu.	35-6† -	48

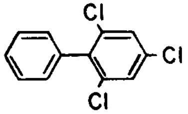
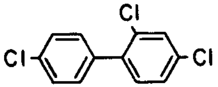
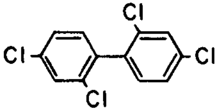
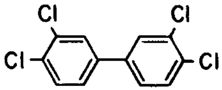
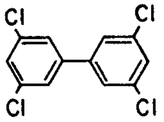
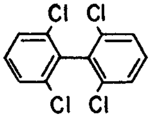
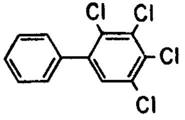
Trichlorobiphenyls						
2,4,6-		2,4,6-Trichloroaniline (I)	A_2 (6)	Col.,TLC, EtOH aqu.	62-3 62.5(6)	51
2,4,4'-		4,4'-Dichloro-2-nitrobiphenyl (18) ↓	F			
		2-Amino-4,4'-dichlorobiphenyl	C	MeOH aqu.	57-8 55(19)	53
Tetrachlorobiphenyls						
2,4,2',4'-		2,2'-Dichlorobenzidine (20)	C(20)			
		or				
		2,4-Dichloroiodobenzene (21)	B_1 (21)	Dist.,Col., EtOH aqu.	41 41-42(22) 83(21)	58
3,4,3',4'-		3,4,3',4'-Tetraaminobiphenyl (VI)	C			
		or				
		3,3'-Dichlorobenzidine (VIII)	C(20)	TLC, EtOH aqu.	173 172(20)	44

TABLE (contin.)

Compound[‡]		Preparation			Physical data	
Name	Formula	Starting Material (Sources[§],[+])	Method[*]	Purification[‡‡]	m.p.[**] °C Found Lit.	R_f[§§]×100
3,5,3',5'-		3,5,3',5'-Tetrachlorobenzidine (20)	D(20)	TLC, MeOH, hexane	164 162(20)	65
2,6,2',6'-		2,6-Dichloroaniline (I) ↓	G			
		2,6-Dichloroiodobenzene	B_1	Col., EtOH,aqu.	198 198(20)	40
2,3,4,5-		2,3,4,5-Tetrachloronitrobenzene (IV) ↓	F			
		2,3,4,5-Tetrachloroaniline	A_1	Col., MeOH	91 92(23)	48

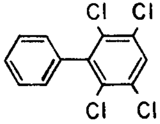
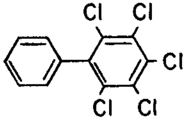
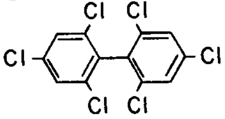
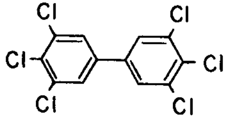
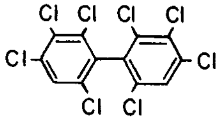
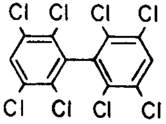
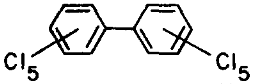
2,3,5,6-		2,3,5,6-Tetrachloronitrobenzene (I) ↓	F			
		2,3,5,6-Tetrachloroaniline	A_1	Col., hexane	79 78-79(24)	50
Pentachlorobiphenyl						
2,3,4,5,6-		Pentachloronitrobenzene (I) ↓	F	Col. MeOH	$123^{\dagger}$ -	51
		Pentachloroaniline	A_2			
Hexachlorobiphenyls						
2,4,6,2',4',6'-		2,6,2',6'-Tetrachlorobenzidine (20)	C(20)	Col., MeOH/EtOH	112-3 112.5(21)	69
		or				
		2,4,6-Trichloroiodobenzene (21)	B_1 (21) B_2			

TABLE (contin.)

Compound‡		Preparation			Physical data	
					m.p.** °C	
Name	Formula	Starting Material (Sources§,+)	Method*	Purification‡+	Found Lit.	R_f§§×100
3,4,5,3',4',5'-		3,3',5,5'-Tetrachlorobenzidine (20)	C(20)	TLC, EtOH aqu.	201-2 198(20)	54
Octachlorobiphenyls						
2,3,4,6,2',3',4',6'-		3,3'-Diamino-2,4,6,2',4',6'-tetrachlorobiphenyl (25)	C	TLC, EtOH	132† -	70
2,3,5,6,2',3',5',6'-		2,3,5,6-Tetrachloronitrobenzene (I) ↓ 2,3,5,6-Tetrachloroaniline ↓ 2,3,5,6-Tetrachloro-1-iodobenzene	F G B_1	TLC, EtOH aqu.	160-1 161(20)	68

Decachlorobiphenyl		Aroclor 1268 (VII)	E(cf.12)	Benzene	305-6 310(20) 296-8°(26)	76

[‡] The following chlorobiphenyls are commercially available (Source[+]): 2-chlorobiphenyl (IV, V, VIII); 3-chlorobiphenyl (IV, V, VIII); 4-chlorobiphenyl (I, IV, V, VIII); 2,2'-dichlorobiphenyl (IV, VIII) and 4,4'-dichlorobiphenyl (I, IV, VIII).

[+] Code for commercial suppliers: I, Aldrich Chem. Co.; II, Sapon Lab.; III, Eastman; IV, Chemical Procurement Labs; V, K&K Lab.; VI, Burdick & Jackson Lab.; VII, Monsanto Chem. Co.; VIII, Pfalz & Bauer Chemicals.

[§] Prepared by method given in reference or commercially available.

[++] TLC = preparative thin-layer chromatography (hexane); Col. = silica column (hexane): MeOH = methanol; EtOH = ethanol; Dist. = distillation at 0.5 mm.

[*] Methods A-F are described in the experimental section. The compound was prepared by a new route where no reference is given.

[**] New compound, when no literature m.p. given.

[§§] In heptane on commercially prepared thin layer plates (Merck silica gel F-274).

[†] Analyses for new compounds. 2,6-Dichlorobiphenyl, calcd. for $C_{12}H_8Cl_2$: C, 64.60; H, 3.61; Cl, 31.78%. Found: C, 64.64; H, 3.46; Cl, 31.45%. 2,3,4,5,6-Pentachlorobiphenyl; calcd. for $C_{12}H_5Cl_5$: C, 44.15; H, 1.54; Cl, 54.30%. Found: C, 43.89; H, 1.56; Cl, 54.16%. 2,3,4,6,2',3',4',6'-Octachlorobiphenyl; calcd. for $C_{12}H_2Cl_8$: C, 33.54; H, 0.47; Cl, 65.99%. Found: C, 33.63; H, 0.37; Cl, 65.68%.

extracted with benzene and the crude material obtained after evaporation of the solvent was purified by the methods given in A_1.

B_2, Using dimethylformamide as solvent - The procedure given in ref. 10 was followed.

C, Sandmeyer Reaction (11)

The chloroaniline was diazotized as given under A_1 and the filtered solution added, dropwise, to a stirred solution of cuprous chloride (10 g for each amino group) in conc. HCl (80 ml) at -5°. The mixture was allowed to warm to 25° and stirred for two more hours. The crude product was extracted with benzene or removed by filtration, washed with water and purified as given under A_1.

D, Deamination

The amino compound was diazotized as given in A_1 and the filtered diazonium salt solution was added, dropwise, to boiling ethanol (5X the volume of diazonium salt solution). The solution was boiled for additional 15 minutes, most of the solvent removed by evaporation and the crystals of the crude chlorobiphenyl that precipitated after cooling were purified by the methods given in the Table.

E, Exhaustive Chlorination (Decachlorobiphenyl) (cf. 12)

A mixture of Aroclor 1268 (2 g) and antimony pentachloride (4 g) was heated at 150°, under anhydrous conditions for 4 hours. After cooling, the crystals were removed by filtration and washed with conc. hydrochloric acid; an aqueous solution of tartaric acid and finally with water.

F, Reduction of Nitro Group

Reductions of nitro groups were carried out by standard procedures, i.e. iron and hydrochloric acid or zinc and aqueous or ethanolic acetic acid.

G, Preparation of Iodo Compound

The iodo compound was prepared from a diazonium salt solution (A_1) and aqueous potassium iodide (1.5 M).

References

1. WIDMARK, G., The OECD Study of Analysis of PCB, Report from the Institute of Analytical Chemistry, Stockholm, Sweden, 1968.
2. SISSONS, D. J. and TELLING, G. M., personal communication.
3. ZITKO, V., HUTZINGER, O. and SAFE, S., Bull. Environ. Contam. Toxicol., in press.
4. SAFE, S. and HUTZINGER, O., Chem. Commun., in press.
5. WEINGARTEN, H., J. Org. Chem. 26, 730 (1961).
6. AUGOOD, D. R., HEY, D. H. and WILLIAMS, G. H., J. Chem. Soc. 44 (1953).
7. FANTA, P. E., Chem. Rev. 38, 139 (1946).
8. FANTA, P. E., Chem. Rev. 64, 613 (1964).
9. BACON, R. G. R. and HILL, H. A. O., Quart. Rev. 19, 95 (1965).
10. KORNBLUM, N. and KENDALL, D. L., J. Amer. Chem. Soc. 74, 5782 (1952).
11. SAUNDERS, K. H., The Aromatic Diazo-Compounds and Their Technical Applications, E. Arnold & Co., London, 1949.
12. WEBER, A. and SÖLLSCHER, C., Ber. 16, 882 (1883).
13. BEAVEN, G. H., DE LA MARE, P. B. D., HASSAN, M., JOHNSON, E. A. and KLASSEN, N. V., J. Chem. Soc. 2749 (1961).
14. GOMBERG, M. and BACHMANN, W. E., J. Amer. Chem. Soc. 46, 2339 (1924).
15. SCHWECHTEN, H. W., Ber. 65, 1605 (1932).
16. CAIN, J. C., J. Chem. Soc. 85, 7 (1904).
17. FICHTER, F. and ADLER, M., Helv. Chim. Acta 9, 279 (1926).
18. SHAW, F. R. and TURNER, E. E., J. Chem. Soc. 285 (1932).
19. RAUDNITZ, H., Ber. 60, 738 (1927).
20. VAN ROOSMALEN, F. L. W., Rec. Trav. Chim. 53, 359 (1934).
21. ULLMANN, F., Ann. Chem. 332, 38 (1904).
22. HALL, D. M. and MINHAJ, F., J. Chem. Soc. 4584 (1957).
23. MCBEE, E. T., DIVELEY, W. R. and BURCH, J. E., J. Amer. Chem. Soc. 77, 385 (1955).
24. BAIN, P. J., BLACKMAN, E. J., CUMMINGS, W., HUGHES, S. A., LYNCH, E. R., MCCALL, E. B. and ROGERTS, R. J., Proc. Chem. Soc. 186 (1962).
25. WHITE, J. and ADAMS, R., J. Amer. Chem. Soc. 54, 2104 (1932).
26. SANDOZ, Belg. Pat. 665,732, Oct. 18, 1965; Chem. Abstr. 64, 19847 (1966).