

Polychlorinated Biphenyls

II.* Synthesis of Some Tetra- and Pentachlorobiphenyls

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The syntheses of eighteen tetra- and pentachlorobiphenyls, most of which are unsymmetrically substituted, are described. Their physical characteristics, including relative retention times in gas-liquid chromatography and their occurrence in commercial PCB-mixtures, as previously reported, are recorded in Table 1.

The occurrence of polychlorinated biphenyls (PCB) in fish and birds from coastal waters was first reported by Jensen¹ and comprehensive reviews dealing with various aspects of the present widespread environmental pollution through PCB have recently been published.^{2,3}

Commercial PCB-mixtures used, *e.g.*, in the electrical industry, contain a number of related compounds with one to ten chlorine atoms in the molecule.^{4,5} Only a restricted number of these constituents have so far been prepared by unambiguous synthetic routes.⁶⁻⁸

The present paper describes the simple synthesis of 3 symmetrically and 15 unsymmetrically substituted tetra- and pentachlorobiphenyls, of interest as reference compounds in analytical work on environmental pollutants. Recently, a synthesis of ¹⁴C-labelled tetrachlorobiphenyls *via* a Gomberg-Bachmann reaction between diazotised 2,4-dichloroaniline-¹⁴C and 1,2-dichlorobenzene was described.⁹ However, this method is not applicable in coupling reactions where the chlorobenzene component is a solid at temperatures close to 0°.¹⁰

In the syntheses of the biphenyls described in Table 1 we have, with two exceptions (*cf.* below), used the method described by Cadogan,¹¹ in which arylation of an aromatic compound is achieved through its reaction at elevated temperatures with a mixture of an aniline and isoamyl nitrite. The six isomeric dichloroanilines and 2,4,5-trichloroaniline were thus coupled with 1,4-di- and 1,2-dichlorobenzene. In the reactions with 1,2-dichlorobenzene, two isomeric biphenyls were formed in a ratio of *ca.* 2:1 as determined by GLC. The coupling

* Part I, *cf.* Ref. 9.

of 3,5-dichloroaniline with 1,2-dichlorobenzene gave substantial amounts of by-products and the Gomberg-Bachmann reaction was chosen as more suitable for that particular coupling. The structure for each individual, isolated component was assigned on the basis of the UV spectrum which in each case revealed the number of substituents in the *ortho*-position to the biphenyl linkage.¹² For pairs of related biphenyls derived from 1,2-dichlorobenzene, the one with the higher number of chlorine atoms *ortho* to the biphenyl linkage had the shortest retention time, in agreement with previous observations.⁴ As expected, this isomer was the one formed in minor amounts in the coupling reaction. It is noteworthy, that throughout the series, all the minor components, on thin layer chromatography on silica gel using hexane as solvent, had slightly lower R_F -values than the major ones.

2,3',5,5'-Tetrachlorobiphenyl is erroneously described in an encyclopaedic work¹³ as having m.p. 162°. The reference given,¹⁴ however, contains no information about this compound, but describes, instead, the synthesis of the isomeric 3,3',5,5'-tetrachlorobiphenyl, m.p. 162°. In the same encyclopaedic work,¹³ 2,3',4,4',5-pentachlorobiphenyl is reported as having m.p. 179°. However, the references cited^{15,16} give no conclusive evidence for this structure.

Saeki *et al.*⁸ recently described a compound erroneously formulated as 2,3',4,4',5-pentachlorobiphenyl, m.p. 82°. The two main products formed in the coupling of 2,4,5-trichloroaniline with 1,2-dichlorobenzene, from reasons given above, must be formulated as 2,3',4,4',5-pentachlorobiphenyl, m.p. 112–113°, and 2,2',3',4,5-pentachlorobiphenyl (minor component), m.p. 81.5–82.5°, respectively (*cf.* Table 1). The NMR-spectrum (100 MHz) of the compound with m.p. 112–113° was also in all parts consistent with the published 220 MHz spectrum of 2,3',4,4',5-pentachlorobiphenyl.⁵

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage. UV spectra were measured in 99.5 % ethanol on a Perkin-Elmer 124 spectrophotometer. 2,3-, 2,5-, 3,4-Dichloroaniline and 2,4,5-trichloroaniline (Koch-Light), 2,6- and 3,5-dichloroaniline (Fluka), and 2,4-dichloroaniline (Schuchardt) were of reagent grade and were purified by crystallization before use. 1,4-Dichlorobenzene (Kebo AB, *purum*), 1,2-dichlorobenzene (Koch-Light, ≥ 99 %), and isoamyl nitrite (Riedel-de Haën, pure, DAB. 6) were used without further purification.

Gas chromatography. The biphenyls were characterized by GLC using a Varian 1400 instrument fitted with an electron capture detector. Glass columns (0.18 × 160 cm) containing 4 % (w/w) SF 96 on Chromosorb W A/W DMCS (100–120 mesh) were used. The retention time of the standard compound, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (*p,p'*-DDE), was kept as close to 24 min as possible. This condition was obtained with a gas flow (nitrogen) of *ca.* 25 ml/min and an oven temperature of *ca.* 160°.

Coupling of di- or trichloroanilines with 1,4-dichlorobenzene. The chloroaniline (0.5 g) was mixed with 1,4-dichlorobenzene (12 g) and the mixture was heated to *ca.* 60°. Isoamyl nitrite (1 ml) was added to the melt with stirring. The reaction mixture was slowly heated to *ca.* 130° and kept at this temperature for 1.5 h. Excess dichlorobenzene was removed by evaporation at 140–150° under a flow of nitrogen. The residue was dissolved in a small amount of hexane:chloroform (1:1) and added to the top of a silica gel (Merck, 0.05–0.2 mm) column (1.5 × 19 cm). Hexane was used as eluant. Evaporation of solvent gave oils which crystallized upon the addition of methanol or ethanol. The yields were in the range of 20–30 %. Recrystallization followed by sublimation *in vacuo* gave the analytical samples (Table 1).

Table 1.

Di- or trichloro- aniline	Dichloro- benzene	Chloro- biphenyl formed	m.p. °C	λ_{\max} nm log ϵ	Analyses ^a % C % H	Occurrence in Aroclors ^b 1242 1254	Relative retention time ^c	
2,3-	1,4-	2,2',3,5'-	49-50 (aqMeOH)	266.5 (sh) 2.97	275.5 283 3.07 3.00	(+)	++	0.46
2,4-	1,4-	2,2',4,5'-	65-66.5 (MeOH)	274 3.08	281.5 2.99	(++)	-	0.41
2,5-	1,4-	2,2',5,5'-	85-86.5 (MeOH) ^d	268 (sh) 3.06	275.5 283.5 3.21 3.16	++	++	0.39
2,6-	1,4-	2,2',5,6'-	103-104.5 (MeOH)	268 (sh) 2.91	275.5 283.5 49.4 3.00 2.91	-	-	0.33
3,4-	1,4-	2,3',4',5'-	104-105 (MeOH) ^e	247 4.21	285 (sh) 3.40	++	++	0.63
3,5-	1,4-	2,3',5,5'-	105.5-106.5 (EtOH)	245 (sh) 3.98	283.5 (sh) 3.25	(+)	(+)	0.51
2,3-	1,2-	2,3,3',4'- 2,2',3,3'-	96-97 (MeOH) ^f 121-122 (EtOH)	251 4.18 271.5 2.88	49.5 2.1 279.5 (sh) 2.80	+	+	0.74 0.54

2,4-	2,3',4,4'-	127-128 (EtOH) ^g	251 4.22	-	-	+	0.65
	2,2',3,4'-	68.5-70 (EtOH)	272.5 280.5 2.95 2.81	49.4 2.2	+	+	0.47
	2',3,4,6'-	Oil	272.5 (sh) 281 (sh) 3.10 2.98	49.6 1.9	-	+	0.50
2,6-	2,2',3,6'-	125.5-127 (MeOH)	267.5 274.5 2.89 2.85	49.5 2.2	-	-	0.38
3,4-	3,3',4,4'-	177-178 (EtOH) ^h	261 4.17	-	(+)	(+)	0.99
	3,3',4,5'-	119-120 (EtOH)	258.5 4.26	49.4 2.1	-	-	0.82
3,5-	2,3,3',5'-	127.5-129 (MeOH)	243.5 280 (sh) 4.00 3.09	49.4 2.1	(+)	-	0.58
2,4,5-	2,2',4,5,5'-	76-77 (EtOH)	275.5 (sh) 281 289 3.11 3.24 3.12	44.0 1.7	+	++	0.80
	2,3',4,4',5-	112-113 (EtOH) ⁱ	251.5 4.21	44.3 1.6	-	++	1.27
2,4,5-	2,2',3',4,5-	81.5-82.5 (subl.) ⁱ	272 281 289.5 2.64 2.70 2.62	44.3 1.7	+	++	0.92

^a Required for C₁₂H₆Cl₄: C 49.4, H 2.1; C₁₂H₆Cl₅: C 44.2, H 1.5. ^b From Ref. 4. Commercial products manufactured by Monsanto Chemicals, containing 42 and 54 % w/w chlorine, respectively. ++: major component, +: minor component, -: not detected. Uncertain results are bracketed. ^c *p,p'*-DDE=1.00. For conditions, see Experimental. ^d Ref. 7, 86.5-87°; Ref. 17, 84-85°. ^e Ref. 18, 103°; Ref. 19, 104°. ^f Also obtained as a minor component in the coupling of 3,4-dichloroaniline with 1,2-dichlorobenzene. ^g Ref. 8, 124°; Ref. 9, 127-128°. ^h Ref. 6, 173°; Refs. 8, 14, 172°. ⁱ See text.

Coupling of di- or trichloroanilines with 1,2-dichlorobenzene. The chloroaniline (1.5 g) was dissolved in 1,2-dichlorobenzene (15 ml) and isoamyl nitrite (2 ml) was added dropwise with stirring at ca. 40°. The mixture was heated to ca. 130° and kept at this temperature for 1.5 h. The work-up was performed as described above, total yield 20–30%. The major products formed in the reaction from 2,3-, 2,4-, 3,4-dichloroaniline and 2,4,5-trichloroaniline, respectively, crystallized upon the addition of methanol or ethanol to the oily crude products. The analytical samples were purified by recrystallization followed by sublimation *in vacuo*.

The biphenyl fractions (ca. 150 mg portions) obtained from the above alcoholic mother liquors were subjected to chromatography on columns (2 × 25 cm) containing silica gel (Merck, < 0.08 mm) with hexane as eluent. The course of the separations was followed by GLC and TLC (Merck, Kieselgel HF₂₅₄, hexane). In all cases the minor components were eluted after the major ones. The analytical samples were purified as above.

The two tetrachlorobiphenyls formed from 2,6-dichloroaniline were obtained in a pure state only through column chromatography of the crude reaction product as described above.

Gomberg-Bachmann coupling of 3,5-dichloroaniline with 1,2-dichlorobenzene. 3,5-Dichloroaniline hydrochloride (1.5 g) was suspended in 1,2-dichlorobenzene (50 ml) and cooled to 0°. A solution of sodium nitrite (6 M, 1.5 ml) was added dropwise with vigorous stirring during 15 min. After another 15 min, a solution of sodium hydroxide (5 M, 9 ml) was added in small portions during 30 min. Stirring was continued for 1.5 h while the reaction mixture was allowed to attain room temperature. After removal of the aqueous phase the dichlorobenzene was evaporated and the residue purified as described above.

The two tetrachlorobiphenyls formed were isolated through column chromatography as described above using hexane:ether (9:1) as eluent. The analytical samples were purified as described above.

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