PCB - synthesis and radioactive labelling (— 4 Cl-atoms) *)

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The toxicity of PCB is almost unknown. Our present knowledge is based on some small scale experiments on rats exposed to PCB for not more than a month. Therefore I found it important to understand what happens to PCB once it enters the body of mammals.

Autoradiography is a specific and fast method for studying the distribution of labelled PCB. My present research deals with the discovery of possible routes for the labelling of PCB. I started with the tetrabiphenyls because they are one of the most common PCBs. The methods used here can be adapted to the synthesis of other polychlorinated biphenyls.

Some remarks on the synthesis of labelled compounds.

Small scale

The synthesis must be carried out on a small scale for two reasons - the cost and the hazards with radioactive material.

Adaptability to a closed system

The hazards with C^{14}-labelled compounds force one to use a synthesis that minimizes the exposure of the personal. Therefore, some possible good chemical solutions might be troublesome when used with C^{14}.

High yield

The expense of the starting material demands a very good yield in each step.

Few starting compounds

The choice of starting material is very restricted. Benzene, nitrobenzen, chlorobenzene and aniline are used as starting materials.

The possible routes for synthesis of labelled PCB are often very well known. However, since many of them originated at the beginning of this century, it means that the syntheses are carried out in at least a 100 gram scale. If one uses those methods and simply scales them down, very often the synthesis will not work at all. A typical example is the industrial production of PCB, in which Cl_2 is introduced into melted biphenyl. This gives you a mixture of chlorinated biphenyls which is not wanted for toxicological studies, and too low a yield in a small scale operation. The same is true for syntheses involving diazotations.

Synthesis 1

nitrobenzene → benzidine → PCB

Nitrobenzene is reduced with zink dust and aqueous sodium hydroxide to give hydrazobenzene. It will undergo rearrangement to benzidine with hydrochloric acid. Benzidine will be acetylated by boiling for two hours in acetic acid. After cleaning, the diacetylbenzidine is chlorinated with chlorine in acetic acid solution and 3, 5, 3', 5'-tetrachloro-N, N'-diacetylbenzidine is formed as a flocculent precipitate. It can be converted to tetrachlorobiphenyl.

Synthesis 2

Bromobenzene $\xrightarrow{\text{Step 1}}$ biphenyl $\xrightarrow{\text{Step 2}}$ PCB

Step 1

There are three synthesis from bromobenzene to biphenyl that we have studied.

I Bromobenzene is allowed to react with solid sodium for 28 hours. The yield was 29%.

II Bromobenzene was heated with copper bronze in an ampul at 210° for 17 hours. GLC gave the composition 5:1 (bromobenzene: biphenyl).

III This is a Grignard reaction that starts with bromobenzene.

$$C_6H_5MgBr + CoCl_2 \longrightarrow C_6H_5Co\,Cl + MgBrCl$$
$$2\,C_6H_5CoCl \longrightarrow C_6H_5C_6H_5 + CoCl$$
$$CoCl + C_6H_5Br \longrightarrow CoClBr + C_6H_5$$
$$C_6H_5 \cdot \longrightarrow C_6H_6 + C_6H_5C_6H_5 + \text{polymers}$$

Using GLC we got bromobenzene : biphenyl : higher polymers : benzene 12,5 : 18,5 : 2 : 1. The literature reports 86% yield. (Ref. 2).

Step 2

The chlorination of biphenyl was carried out with Cl_2 in acetic acid - Cl_2 acetic acid ; carbon tetrachloride (1 : 3); Cl_2 in silver sulfate and sufuric acid in carbon tetrachloride; sulfuryl chloride: silver perchlorate and chloroacetate; perchloric acid and acetic acid. Of these methods, Cl_2, silver sulfate and sulfuric acid in carbon tetrachloride gave the best result although the method is not satisfactory. After 22 hours all biphenyl was converted to monochlorobiphenyl and dichlorobiphenyl and after 13 days the end product was dichlorobiphenyl and trichlorphenyl in the proportion 1 : 3.
(Ref. 3)

Synthesis 3

1-Chloro-2,4,dinitrobenzene → tetranitrobiphenyl

By Ullman coupling in copper bronze, 1-chloro-2,4-dinitrobenzene is condensed to 2,4,2',4'-tetranitrobiphenyl.

Synthesis 4

2, 4-dichloroaniline → PCB

2, 4-dichloroaniline is diazotised in concentrated sulfuric acid. The azocompound is put into the potassium iodide solution drop by drop. 1-iodo-2, 4-dichlorobenzene formed gives 2, 4, 2', 4'-tetrachlorobiphenyl with an Ullman coupling.

The yields from different steps have been studied with GLC measuring only the starting material and the end products. These values do not give the practical yield of the pure product and therefore only serve as a tool for discovering the best condition for a specific synthesis. The present work concerns the procedures for purifying the products and modifying the methods in order to get a better yield. At the moment, it is still too early to say which one of the syntheses that will give the best yield and will best satisfy the demands given above.

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