Cellulose Bound Chlorophenols II: Preparation and Characterization of Phenyloxycarbonylpentanoyl Celluloses Dependence of Substitution on Chlorophenol Structure*

PETER MAIR, MÜFIT BAHADIR, and FRIEDHELM KORTE,
Institut für Ökologische Chemie der Gesellschaft für Strahlen- und Umweltforschung, D-8042 Neuherberg and Lehrstuhl für Ökologische Chemie der Technischen Universität München, D-8050 Freising-Weihenstephan

Synopsis

New types of polymeric phenols (including the fungicide PCP) are prepared by linking phenol and different chlorophenols to cellulose via ester bonds using adipic acid as bridging molecule. Monophenylesteracid chlorides of adipic acid are prepared as intermediates. The yield of esterification of cellulose with these compounds depends in a complicated manner on size and chlorosubstitution pattern of the phenolic substituents. It is tentatively assumed that hydrogen bonding between chlorophenol and cellulose is an important factor. The polymeric PCP ester showed fungicidal activity in an agar plate test.

INTRODUCTION

Conventional technologies for the application of biocides lead to fast dissipation of low molecular weight bioactive substances.[1] Besides economical disadvantages, these wasteful practices bring about an ubiquitous presence of bioactive compounds with possibly dangerous consequences for mankind and the biosphere.

The approach of "controlled release technology" (CRT), whose general principles are reviewed in several papers,[2,3] might provide a way to avoid these disadvantages and to gain additional benefits.

One realization of CRT is the covalent attachment of the bioactive agent to a macromolecular backbone. We are investigating the utility of cellulose as a carrier for pesticides, because it is an ecologically safe and a renewable raw material of widespread use. Presently we are studying different linkages and different spacer molecules between polymer and pesticides, since it has been shown that biological activity depends strongly on these parameters.

While organo–mercury compounds show their biocidal activity in the bound state,[4] pentachlorophenylethers of cellulose are not effective.[5] In this study we are reporting on the preparation of compounds, which contain phenylesters bound to cellulose via adipic acid (phenyloxycarbonylpentanoyl celluloses

*Part I: see Ref. 5.

Journal of Applied Polymer Science, Vol. 34, 1345–1351 (1987)
© 1987 John Wiley & Sons, Inc. CCC 0021-8995/87/041345-07$04.00

TABLE I
Substitution Pattern of the Used Phenols

Code		a	
Isomer		Phenol	
Code	b	c	d
Isomer	2-Chloroph.	3-Chloroph.	4-Chloroph.
Code	e	f	g
Isomer	2,4-Dichloroph.	2,6-Dichloroph.	3,5-Dichloroph.
Code	h	i	j
Isomer	2,4,5-Trichloroph.	2,4,6-Trichloroph.	3,4,5-Trichloroph.
Code		k	
Isomer		PCP	

III). Ten different chlorophenols and phenol (listed in Table I) have been used to investigate the influence of chlorosubstitution on the reaction yield (DS*). The biological activity of pentachlorophenyloxycarbonylpentanoylcellulose was tested in an agar plate assay with *Trichoderma viride*. The results of hydrolysis experiments with the PCP-derivatives will be published in a forthcoming paper.[6]

EXPERIMENTAL

Infrared (IR) spectra were recorded on a Perkin-Elmer spectrophotometer 1400, nuclear magnetic resonance (NMR) spectra on a Bruker WP 80 CW. To determine the DS of polymeric products (III), 10 mg of the material was hydrolyzed in MeOH/1 N NaOH (1:1 by volume) for 30 min at reflux temperature. The pH of the hydrolysate was adjusted to 2 with conc. HCl and the volume brought to 100 mL with MeOH. Phenol concentrations were determined by high performance liquid chromatography (HPLC).

A reversed-phase column (ODS Hypersil 5 μm, 4.6 × 250 mm), a WISP Autosampler (Waters), and a 1040 M diode array detection system (Hewlett Packard) were used. The eluent compositions for different phenols are listed in Table II, together with the resulting capacity factors (k'), obtained from Eq. (1)

$$k' = \frac{t_r - t_o}{t_o} \tag{1}$$

where t_r (min) is the retention time and t_o (min) the dead time.

Phenyladipoyl chlorides (I)

A method to prepare phenyloxalylchloride was adopted.[7] All steps were done in dried solvents under exclusion of moisture. Phenol, 37 mmol dissolved together with 37 mmol (5.2 mL) triethylamine in 75 mL CCl_4 were added dropwise to a cooled (−10 to 0°C) mixture of 185 mmol (27 mL) adipoylchloride in 50 mL CCl_4 and the mixture was stirred at room temperature for 1 h. The precipitate ($Et_3N \cdot HCl$, quantitative yield) was filtered off by suction. Solvent and excess adipoylchloride were removed under reduced pressure (1400 Pa and

*DS: Degree of substitution (mol phenyloxycarbonylpentanoyl substituents/mol anhydroglucose units).

TABLE II
Eluent Composition for HPLC of Phenols

Phenol	Eluent	k'
Phenol,		1.54
2-Chlorophenol,		2.36
3-Chlorophenol,	MeOH:H_2O = 60 : 40	2.94
4-Chlorophenol		2.77
2,4-Dichlorophenol,		2.67
2,6-Dichlorophenol,	MeOH:H_2O = 70 : 30	2.00
3,5-Dichlorophenol		3.52
2,4,5-Trichlorophenol,		2.06
2,4,6-Trichlorophenol,	MeOH:H_2O = 80 : 20	2.01
3,4,5-Trichlorophenol		2.63
PCP	MeOH:buffer[a] = 90 : 10	2.10

[a] Phosphate buffer, pH = 2.5, 5 m*M*.

70 Pa, respectively). The resulting products were used without further purification. Residual adipoylchloride was determined by NMR and amounted always to less than 10 mol%. An approximate amount of 10% or less of the corresponding diester was found by thin layer chromatography (TLC). Aliquots (3 mmol) of the crude products (I) were reacted with methanol and purified by column chromatography (Lobar prepacked column, LiChroprep Si 60, 2.5 × 24 cm (Merck), toluene/ethylacetate 7 : 3, 10 mL/min). The data from elemental analysis and spectroscopy of the resulting phenylmethyladipates (II) prove the supposed structure of (II) and, hence (I). A compilation of all spectroscopic data can be obtained from the authors.

Phenyloxycarbonylpentanoylcellulose (III)

A method to prepare oxalic esters of cellulose[8] was optimized. First, 0.5 g (3 mmol anhydroglucose units) cellulose (filter cotton wool, Macherey & Nagel MN 101; for PCP derivatives also filter papers ϕ 2 cm, Schleicher & Schüll Nr.

TABLE III
Phenol Contents (wt% Hydrolizable Phenol in Modified Cellulose) and Characteristic IR Bands of Cellulose Esters (III)

Code	Phenol content wt%	IR absorption (KBr, cm^{-1}) COOAr	COOCell	C=C
a	36.4	1755	1730	1590, 1490, 1455
b	34.2	1758	1730	1580, 1742
c	31.3	1755	1730	1585, 1470
d	27.6	1755	1730	1485
e	37.4	1760	1730	1580, 1470
f	18.3	1760	1730	1572, 1445
g	30.1	1760	1735	1578, 1428
h	5.4	1765	1730	1560, 1445
i	14.9	1765	1730	1560, 1445
j	29.0	1758	1730	1581, 1562, 1425
k	1.9	1730		—

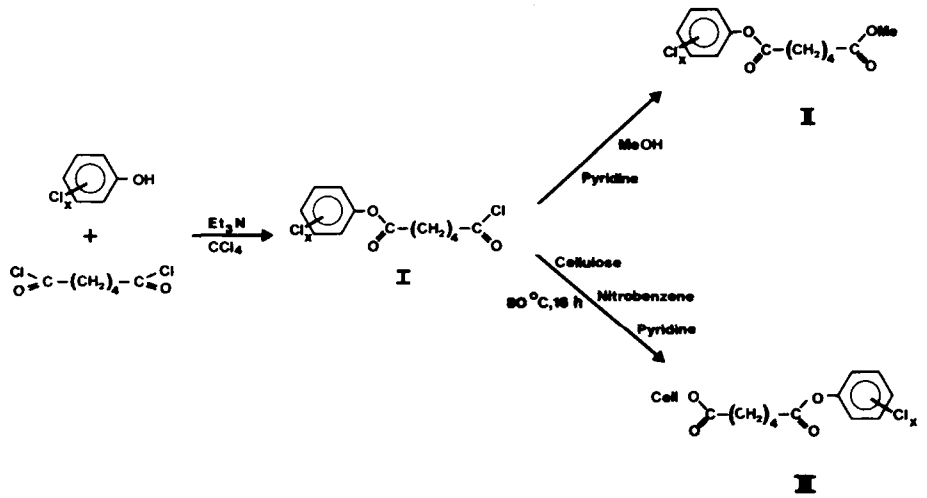

Fig. 1. Reaction sequence to phenyloxycarbonylpentanoyl cellulose (III).

595) were swollen in pyridine at 80°C for 24 h. Cellulose was filtered by suction and dispersed in 10 mL nitrobenzene and 1.6 mL pyridine. A solution of the phenyladipoylchloride (I) in 20 mL nitrobenzene was added dropwise under cooling. The reaction mixture was stirred for 16 h at 80°C and poured in MeOH. The products were filtered, purified with acetone in a soxhlet extractor, and dried at 70°C/140 Pa. Important analytical data can be found in Table III.

Round filter papers treated the same way as cotton wool with pentachlorophenyladipoylchlorid contained 4 wt% PCP. The modified filters were used as Polymeric samples in an agar plate assay with the fungus *T. viride* as described earlier.[5]

RESULTS AND DISCUSSION

We used a straightforward two-step procedure to prepare the polymeric phenylesters (III), which have not been reported previously (Fig. 1). In order to suppress diester formation, a fivefold excess of adipoylchloride had to be used in the esterification reaction. The reaction proceeded smoothly and yielded approximately 90% of the phenylestermonochlorides (I), as shown by spectroscopic data and the preparation of the mixed esters (II).

A pyridine treatment was used to exchange crystal water and to activate the cellulose for esterification.[9] While the reaction mixture turned dark brown during the polymer analogous esterification due to side reactions, the purified products (III) showed only a slightly gray to brown color and had retained their fibrous appearance.

To illustrate eventually important steric factors, the results obtained from the synthesis of 11 phenyloxycarbonylpentanoyl celluloses are shown in Figure 2 grouped into three subfigures. Each of these subplots represents the results obtained with polymeric phenylderivatives having the same number of chloro-substituents in *ortho* position to the phenolic oxygen. Thus the DS of polymeric phenylesters IIIa, c, d, g, j, will be found in Figure 2A, IIIb, e, h in

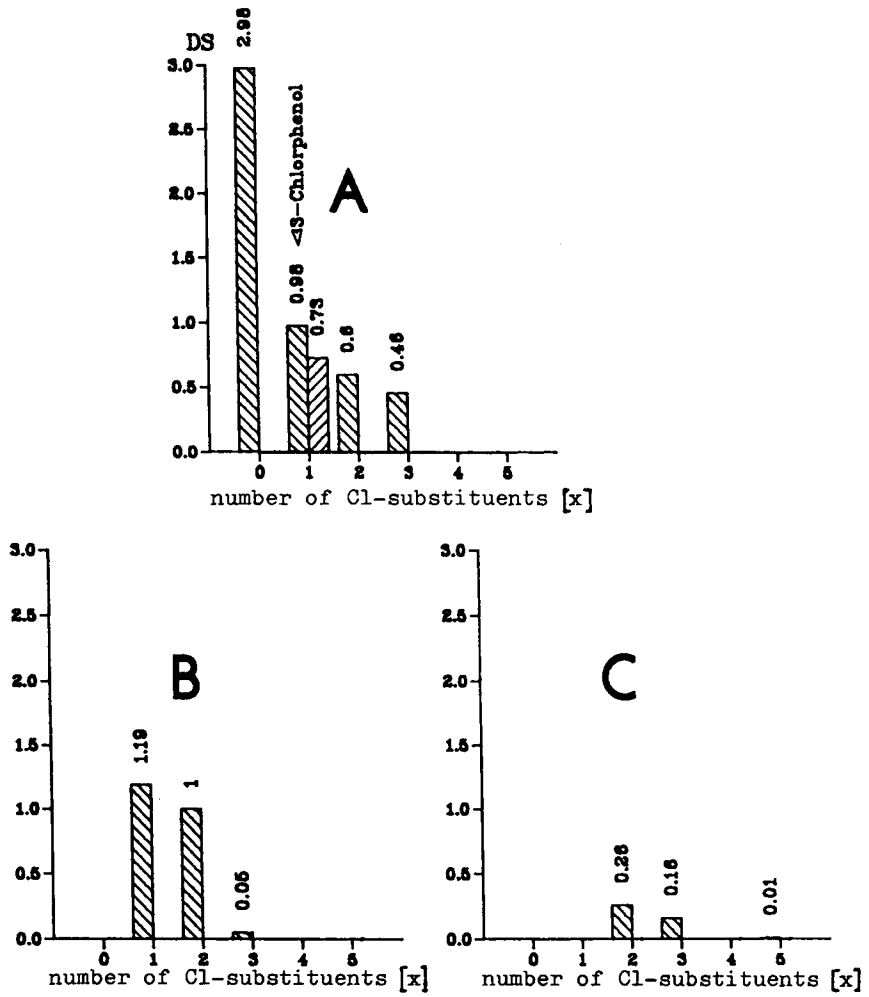

Fig. 2. Dependence of DS of (III) on substitution pattern of the chlorophenols: *A*: No *ortho* substituent; *B*: one *ortho* substituent; *C*: two *ortho* substituents.

2B, and IIIf, i, k in 2c. As can be seen clearly from Figure 2, the DS of the products varies considerably with the different chlorophenols. Not only is a decrease of DS observed with higher chlorinated phenols, but there is also a modulation of DS between isomers.

Other authors[8,10] almost invariably obtained DS values between 2 and 3 in esterification reactions. Since they used long-chain aliphatic or small aliphatic–alicyclic acid chlorides without heterosubstituents, those results can be compared with ours only cautiously.

In our experiments, the separation of the reaction center from the aromatic substituent by 4 sp^3-hybridized C atoms and a carbonyl function precludes any influence of electronic effects. Obviously the size of the phenyl-adipoylchlorides (I) plays a role in determining DS. Larger molecules might diffuse more slowly to reactive OH groups in the lattice of the cellulose fibers. In any group of (I) (0, 1 or 2 chlorosubstituents in *ortho* position to the

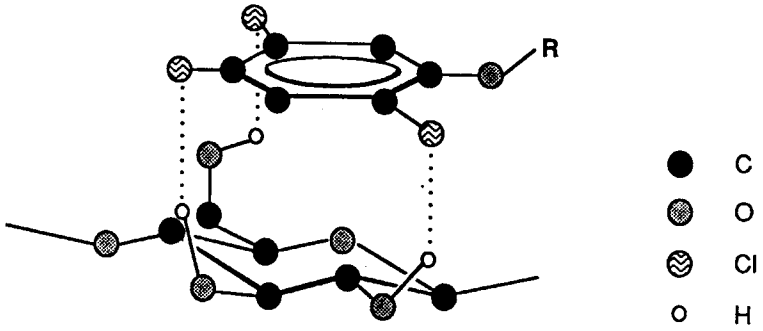

Fig. 3. Possible formation of H bonds between (Ih) and an anhydroglucose unit of cellulose.

phenoloxygen) there is indeed a decrease of DS with increasing number of chlorosubstituents and, hence size. But between the groups certain peculiarities are observed. DS varies for example strongly with the 3 monochlorophenyl derivatives (Ib–d), although the molecular dimensions of the 3 compounds are quite similar. Just the 2-chlorophenyladipoylchloride (Ib) yields the highest DS, though it should be somewhat bulkier than the 3- and 4-chloroisomers, since the *ortho* substituent does not allow a coplanar alignment of phenyl ring and carboxylic group. Similar arguments can be applied to the dichloro- and trichloro-isomers.

After studying molecular models of the reactants, we propose that differentiated hydrogen bonding between the chlorosubstituted aromatic part of the phenyladipoylchlorides and the cellulose matrix to be of utmost importance in determining DS in (III). As an example, Figure 3 shows the molecular arrangement of an anhydroglucose unit and the aromatic moiety of 2,4,5-trichlorophenyladipoylchloride (Ih), which leads to the formation of three O¨H¨Cl-bridges. On the other hand, only two of such H-bonds are possible with the 2,4,6-trichloroisomer (Ii). Finally, only one O¨H¨Cl bridge can exist at any one moment between the phenyl ring of 3,4,5-trichlorophenyladipoylchloride (Ij) and the cellulose backbone. Thus, in this picture, the increasing number of O¨H¨Cl bonds leads through an increased entanglement of the acid chlorides in the polymeric network to a reduced diffusion of the monomeric reactants to the reaction sites, and consequently, to a reduced DS.

It fits into this concept, that phenyladipoylchloride (Ia), which cannot form O¨H¨Cl bridges at all, reacts almost quantitatively with cellulose. On the other end of the observed range of DS values stands the PCP derivative (Ik), which can form a maximum of H bonds in different spatial arrangements. This interaction combined with the large size of the PCP substituent allows only the covalent attachment of 1.9 wt% of the fungicide to the cellulose matrix.

In spite of that low binding efficiency, a biological effect of the modified cellulose (IIIk) could be demonstrated in agar plate assays. While untreated control filter papers were overgrown completely in 3 to 10 days and positive controls impregnated with 200 ppm monomeric PCP produced a zone of inhibition of fungal growth around the filters, the polymeric PCP samples were protected against fungal attack for at least 16 days. However, the

polymeric fungicide did not exert a visible influence on the growth of the microorganisms on the remaining agar plate surface. The fungus grew during all tests just up to the edge of the samples.

The same preparative route used for the polymeric PCP esters (IIIk) was followed using oxalic and succinic acid as bridging molecule, but no useful products could be obtained. Even when reacting a 20-fold excess of oxalyl chloride with pentachlorophenol, the phenyloxalyl chloride could never be isolated. Instead, a precipitate was obtained, which proved to be di(pentachlorophenyl)oxalate by IR, mass spectroscopy (MS), and elemental analysis. Pentachlorophenylsuccinyl chloride and its methyl ester could be produced by the mentioned reactions. However, the pyridine-catalyzed esterification of cellulose with the succinyl semichloride was accompanied by a great number of side reactions. Only a black powdery product with a PCP content of 2% (DS = 0.01) resulted. The powdery appearance of this derivative shows that the cellulose had been heavily degraded.

References

1. G. G. Allan and J. F. Friedhoff, *J. Macromol. Sci., Chem.*, **A10**, 223–244 (1976).
2. C. L. McCormick, K. W. Anderson, and B. H. Hutchinson, *J. Macromol. Sci., Rev.*, **C22**, 57–87 (1982–1983).
3. R. Langer and N. Peppas, *J. Macromol. Sci., Rev.*, **C23**, 61–126 (1983).
4. K. J. Hüttinger, *Chem. Ztg.*, **106**, 415–420 (1982).
5. P. Mair, M. Bahadir, and F. Korte, *J. Appl. Polym. Sci.*, **32**, 5273–5277 (1986).
6. P. Mair, M. Bahadir, and F. Korte, *J. Controlled Release*, submitted for publication.
7. D. Geheb, N. F. Kasanskaja, and F. W. Beresin, *Suom. Kemistil.*, **B44**, 301–307 (1971).
8. G. Frank and W. Caro, *Chem. Ber.*, **63**, 1532–1543 (1930).
9. K. Garves, *TAPPI*, **55**, 263 (1972).
10. A. Grün and F. Wittka, *Angew. Chem.*, **34**, 645–652 (1921).

Received September 29, 1986
Accepted March 25, 1987