

Fiber-Reactive Insecticides for Wool: Phosphorus Esters of 4-[(2-Hydroxyalkyl)thio]phenol

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Thirty-four organophosphorus esters of 4-[(2-hydroxyalkyl)thio]phenol were prepared and screened for insecticidal activity against the wool-digesting insects, *Anthrenus flavipes*, *Tineola bisselliella*, and *Tinea translucens*. The compound that displayed the highest insecticidal activity was *O*-ethyl *S*-*n*-propyl *O*-[4-[(2-hydroxyethyl)thio]phenyl] phosphorothiolate. 2-Bromoacrylic and 3-(vinylsulfonyl)propionic esters were prepared from four of the hydroxy compounds, and their insecticidal activities were determined before and after reaction with the wool. On an equimolar basis, these compounds displayed similar insecticidal activity against wool-digesting insects to the parent hydroxy compounds, and except when the fiber-reactive group was attached to the insecticide by an ester of a secondary alcohol, loss of insecticidal activity due to covalent bonding to the wool was negligible.

Organophosphorus insecticides offer potential for the protection of wool against insect damage, and recently it has been shown (Jones et al., 1981, 1982) that their durability on this fiber can be greatly improved if they are covalently bound to the wool.

Earlier papers (Jones et al., 1982; Jones, 1983b) have described the suitability of *O*,*O*-diethyl *O*-[4-[(2-hydroxyethyl)thio]phenyl] phosphorothionate as an intermediate in the preparation of fiber-reactive esters and ethers. As insecticides are usually applied to wool from a boiling acidic liquor (during dyeing), they must possess good hydrolytic stability. Phosphorus esters based on 4-[(2-hydroxyethyl)thio]phenol are much more stable to these conditions than the phosphorus esters of nitrogen heterocycles (Jones, 1983a) and other phenolic esters containing electron-withdrawing groups (O'Loughlin, 1982). This feature makes this class of compound uniquely suitable as intermediates for wool-reactive insecticides.

As a continuation of this work, a number of phosphorus esters of some 4-[(2-hydroxyalkyl)thio]phenols have been prepared and tested for insecticidal activity against three common wool pests. Fiber-reactive derivatives of four of these compounds were also prepared, and their insecticidal properties were evaluated, both before and after reaction with the wool.

EXPERIMENTAL SECTION

Preparation of Insecticides. The compounds used were prepared by the general methods described below. When required, they were purified by liquid chromatography on a Waters Associates Prep LC System 500 using silica gel as the absorbent and a mixture of ethyl acetate and hexane as the eluting solvent. All compounds were characterized by proton nuclear magnetic resonance spectrometry (60 Hz) and by microanalysis. A tabulation of the ^1H NMR spectra and microanalysis data is provided as supplementary material (see paragraph at the end of paper regarding supplementary material). The structures of the insecticides and the methods of preparation are given in Tables I-III.

Method A. (1) *Preparation of 4-[(2-Hydroxyethyl)thio]phenols.* 2-Chloroethanol (12 g, 0.15 M) was added over 20 min to a refluxing ethanolic solution (150 mL) of the sodium salt of the appropriate 4-mercaptophenol (0.10 M). The mixture was heated under reflux for a further 2 h, cooled, and filtered, and the filtrate was distilled to yield the appropriate 4-[(2-hydroxyethyl)thio]phenol (R^2 ,

R^3 , bp, yield): H, H, 170-174 °C/0.1 mmHg, 88%; H, Cl, 166-172 °C/0.1 mmHg, 80%; Cl, H, 174-179 °C/0.1 mmHg, 72%).

(2) *Phosphorylation of 4-[(2-Hydroxyethyl)thio]phenols.* Acetic anhydride (7.65 g, 0.075 M) was added over 30 min to a refluxing solution of the appropriate 4-[(2-hydroxyethyl)thio]phenol (0.075 M) in formic acid (98-100%, 50 mL). The mixture was heated under reflux for 1 h and the acids were removed at 80 °C under reduced pressure. Anhydrous toluene (75 mL), the appropriate organophosphorus chloridate (0.075 M), and 4-(dimethylamino)pyridine (0.5 g, 0.004 M) were added to the residue, and the mixture was stirred while anhydrous triethylamine (8.08 g, 0.08 M) was added dropwise. The mixture was heated to 60 °C and, after 1 h, filtered. The filtrate was concentrated at 50 °C under reduced pressure, dissolved in ethanol (100 mL), and added to an aqueous solution of potassium carbonate (11 g in 30 mL of H_2O). This mixture was stirred at 20 °C for 5 h, the ethanolic layer was separated, and the ethanol was removed. The residue was taken up in toluene (100 mL), washed with dilute hydrochloric acid (2 M, 3 × 20 mL), aqueous sodium carbonate (1 M, 2 × 20 mL), and water (2 × 30 mL), and dried over MgSO_4 . The solvent was then removed.

Method B. *O*-Alkyl *S*-alkyl *O*-[4-[(2-hydroxyethyl)thio]phenyl] phosphorothiolates were prepared by the action of potassium hydrogen sulfide on the appropriate *O*,*O*-dialkyl *O*-[4-[(2-hydroxyethyl)thio]phenyl] phosphorothionate followed by alkylation with the appropriate alkyl halide (Beriger and Drabek, 1976).

Method C. Triethylamine (2.20 g, 0.02 M) was added dropwise to a solution of the appropriate phosphorus chloridate (0.02 M), 4,4'-dihydroxydiphenyl disulfide (2.5 g, 0.01 M), and 4-(dimethylamino)pyridine (0.61 g) in toluene (50 mL). The reaction mixture was stirred, maintained at 60 °C for 1 h, and filtered. The filtrate was washed successively with dilute hydrochloric acid (2 M, 2 × 20 mL), sodium carbonate solution (1 M, 3 × 20 mL), and water (2 × 30 mL), and dried over MgSO_4 . The solvent was then removed. The crude phosphorylated disulfide was taken up in dioxane (30 mL) containing dilute hydrochloric acid (2 M, 3 mL), the mixture was purged with N_2 , and tributylphosphine (87%, 2.32 g, 0.02 M) was added. After 30 min the mixture was diluted with toluene (50 mL) and extracted with aqueous sodium hydroxide (2 M, 2 × 50 mL). The aqueous extracts were combined, acidified with dilute HCl to pH 3, and extracted with diethyl ether (3 × 50 mL). The organic layers were combined, ethanolic (50 mL) NaOH (1 g) and the appropriate epoxide (0.03 M) were added, the mixture was stirred at

Table I

compd no.							method	yield, %
	R ¹	R ²	R ³	X	R ⁴	R ⁵		
1	-CH ₂ -	H	H	O	C ₂ H ₅ O-	C ₂ H ₅ O-	A	82
2	-CH ₂ -	H	H	O	<i>n</i> -C ₃ H ₇ O-	<i>n</i> -C ₃ H ₇ O-	A	71
3	-CH ₂ -	H	H	S	CH ₃ O-	CH ₃ O-	A	90
4	-CH ₂ -	H	H	S	C ₂ H ₅ O-	C ₂ H ₅ O-	A	95
5	-CH ₂ -	H	H	S	<i>n</i> -C ₃ H ₇ O-	<i>n</i> -C ₃ H ₇ O-	A	68
6	-CH ₂ -	H	H	S	C ₂ H ₅ O-	<i>n</i> -C ₃ H ₇ O-	A	75
7	-CH ₂ -	H	H	O	C ₂ H ₅ O-	CH ₃ S-	B	82
8	-CH ₂ -	H	H	O	C ₂ H ₅ O-	C ₂ H ₅ S-	B	78
9	-CH ₂ -	H	H	O	C ₂ H ₅ O-	<i>n</i> -C ₃ H ₇ S-	B	83
10	-CH ₂ -	H	H	O	C ₂ H ₅ O-	<i>i</i> -C ₃ H ₇ S-	B	71
11	-CH ₂ -	H	H	O	C ₂ H ₅ O-	CH ₂ =CHCH ₂ S-	B	70
12	-CH ₂ -	H	H	O	C ₂ H ₅ O-	<i>n</i> -C ₄ H ₉ S-	B	86
13	-CH ₂ -	H	H	O	C ₂ H ₅ O-	<i>n</i> -C ₅ H ₁₁ S-	B	73
14	-CH ₂ -	H	H	O	C ₂ H ₅ O-	<i>n</i> -C ₆ H ₁₃ S-	B	65
15	-CH ₂ -	H	H	O	<i>n</i> -C ₃ H ₇ O-	C ₂ H ₅ S-	A	58
16	-CH ₂ -	H	H	O	<i>n</i> -C ₃ H ₇ O-	<i>n</i> -C ₃ H ₇ S-	A	63
17	-CH ₂ -	H	H	S	C ₂ H ₅ O-	C ₂ H ₅ S-	A	54
18	-CH ₂ -	H	H	S	C ₂ H ₅ O-	<i>n</i> -C ₃ H ₇ S-	A	78
19	-CH ₂ -	H	H	S	C ₂ H ₅ O-	<i>n</i> -C ₄ H ₉ S-	A	75
20	-CH ₂ -	H	H	O	C ₂ H ₅ -	C ₂ H ₅ O-	A	81
21	-CH ₂ -	H	H	O	C ₆ H ₅ -	C ₂ H ₅ O-	A	78
22	-CH ₂ -	H	H	S	C ₆ H ₅ -	C ₂ H ₅ O-	A	86
23	-CH ₂ -	H	H	O	(CH ₃) ₂ N-	C ₂ H ₅ O-	A	74
24	-CH(CH ₃)-	H	H	S	C ₂ H ₅ O-	C ₂ H ₅ O-	C	85
25	-C(CH ₃) ₂ -	H	H	S	C ₂ H ₅ O-	C ₂ H ₅ O-	C	89
26	-CH(CH ₃)-	H	H	S	C ₂ H ₅ O-	<i>n</i> -C ₃ H ₇ S-	C	62
27	-CH(CH ₂ CH ₃)-	H	H	S	C ₂ H ₅ O-	C ₂ H ₅ O-	C	81
28	-CH ₂ -	Cl	H	S	C ₂ H ₅ O-	C ₂ H ₅ O-	A	92
29	-CH ₂ -	H	Cl	S	C ₂ H ₅ O-	C ₂ H ₅ O-	A	95
30	-CH ₂ -	Cl	H	S	C ₂ H ₅ O-	<i>n</i> -C ₃ H ₇ S-	A	81
31	-CH ₂ -	H	Cl	S	C ₂ H ₅ O-	<i>n</i> -C ₃ H ₇ S-	A	83

Table II

compd no.			
	X	R ⁵	yield, %
32	S	C ₂ H ₅ O-	98
33	O	<i>n</i> -C ₃ H ₇ S-	92
34	S	<i>n</i> -C ₃ H ₇ S-	86

Table III

compd no.				
	R ⁷	R ⁵	X	yield, %
R ⁶ = CH ₂ =CHSO ₂ (CH ₂) ₂ -				
35	-H	C ₂ H ₅ O-	S	78
36	-CH ₃	C ₂ H ₅ O-	S	65
37	-H	<i>n</i> -C ₃ H ₇ S-	O	82
38	-H	<i>n</i> -C ₃ H ₇ S-	S	80
R ⁶ = CH ₂ =CBr-				
39	-H	C ₂ H ₅ O-	S	74
40	-CH ₃	C ₂ H ₅ O-	S	68
41	-H	<i>n</i> -C ₃ H ₇ S-	O	71
42	-H	<i>n</i> -C ₃ H ₇ S-	S	76

20 °C for 3 h, washed with water (2 × 50 mL), and dried over MgSO₄, and the solvent was removed.

Preparation of Sulfoxides. These were prepared by the action of hydrogen peroxide on the appropriate sulfide as described elsewhere (Bayer, 1959).

Preparation of Fiber-Reactive Esters. These were prepared by reacting either 3-[(2-chloroethyl)sulfonyl]-propionyl chloride or 2,3-dibromopropionyl chloride with

the appropriate hydroxyorganophosphorus compound in the presence of a tertiary amine as described previously (Jones, 1983b).

Treatment of Fabric To Determine the Minimum Level Required To Inhibit Feeding Damage. Known amounts of insecticide were applied dropwise to wool fabric from an acetone solution. After the acetone had evaporated these fabrics were bioassayed, as described below, to determine the minimum level of the insecticide required.

Insect Testing. Insect-resist effectiveness was evaluated by assay with larvae of the common clothes moth (*Tineola bisselliella*, Hummel), the case-bearing clothes moth (*Tinea translucens*, Meyrick), and the furniture carpet beetle (*Anthrenus flavipes*, Le Conte) according to the fabric weight loss method as described in AATCC Standard Test Method 24-1977 (American Association of Textile Chemists and Colorists, 1979). By this standard, wool is considered resistant to insects if the feeding damage does not exceed 8 mg, provided that the feeding damage of an untreated control is 30 mg or more.

Application of Fiber-Reaction Insecticide to Wool Fabric from an Aqueous Emulsion. The required amount of insecticide was dissolved in a solution of an ethoxylated nonylphenol containing 13 ethylene oxide units (Teric N13, ICI) (0.01 g) and calcium dodecylbenzenesulfonate (Alkanate CS, ICI) (0.01 g) in xylene (0.5 mL) and blended with water (49 mL) in a high-speed blender. This emulsion was applied to wool fabric (25 g) from an Ahiba Turbomat laboratory dyeing machine. The fabric package was wetted out and immersed in an aqueous solution (450 mL) of ammonium sulfate (1.0 g) and acetic acid (0.25 g) at 40 °C, and the liquor was circulated. The emulsified insecticide was then added, and the liquor was held for 10 min at 40 °C and then raised to 100 °C over 30 min and maintained at this temperature for 3 h. The

Table IV. Insecticidal Activity of Compounds 1-31 against Wool-Eating Insects

compd no.	min concn, mg/g of wool, to control feeding damage due to		
	<i>A. flavipes</i>	<i>T. bisselliella</i>	<i>T. translucens</i>
1	0.05	2.0	>2.0
2	1.5	>2.0	>2.0
3	1.0	1.0	>2.0
4	0.3	0.5	1.0
5	0.7	>2.0	>2.0
6	0.4	0.7	1.0
7	1.5	1.5	>2.0
8	0.5	0.4	0.5
9	0.02	0.03	0.04
10	0.3	0.04	0.2
11	0.5	0.1	1.20
12	0.3	0.4	0.07
13	0.6	0.7	0.2
14	1.2	1.5	1.0
15	1.5	>2.0	>2.0
16	0.2	0.6	0.5
17	0.7	>2.0	>2.0
18	0.06	0.07	0.4
19	0.3	0.5	0.4
20	0.2	1.0	>2.0
21	1.0	>2.0	>2.0
22	1.2	>2.0	>2.0
23	1.3	>2.0	>2.0
24	0.8	0.5	0.5
25	0.5	2.0	>2.0
26	0.2	0.06	0.2
27	0.12	0.7	0.6
28	0.3	0.3	0.7
29	0.3	0.3	1.0
30	0.08	0.1	0.3
31	0.07	0.08	0.3
32	0.5	0.9	1.2
33	0.05	0.07	0.04
34	0.1	0.7	0.7

treated fabric was removed, hydroextracted, and air-dried.

Any unreacted insecticide was removed from the wool by a 3-h Soxhlet extraction with an azeotropic mixture of benzene, methanol, and water (70:26:4). The amount of insecticide bound to the wool was then determined by gas chromatography as described below.

Analysis of Insecticide on the Wool. *O,O*-Diethyl phosphorothionates on wool were converted to *O,O*-diethyl *S*-methyl phosphorothiolate and *O*-ethyl *S-n*-propyl phosphorothiolothionates on wool were converted to *O*-ethyl *S*-methyl *S-n*-propyl phosphorodithiolate. These derivatives were determined by gas chromatography as described previously (Jones, 1983a).

O-Ethyl *S-n*-propyl phosphorothiolates on wool were converted to *O*-ethyl *O*-methyl *S-n*-propyl phosphorothiolate as follows: Duplicate samples of wool (0.200 g) were dissolved in aqueous NaOH (2.5 M, 4 mL) at 70 °C for 20 min, cooled, and acidified with concentrated HCl (1.5 mL) and NaCl (2 g) and a mixture of acetonitrile-diethyl ether (1:1, 4 mL) was added. The mixture was shaken and centrifuged, and an aliquot of the organic phase (2 mL) was treated with ethereal diazomethane (0.25 M, 0.5 mL). The resulting *O*-ethyl *O*-methyl *S-n*-propyl phosphorothiolate was determined by gas chromatography essentially as described previously (Jones, 1983a).

RESULTS AND DISCUSSION

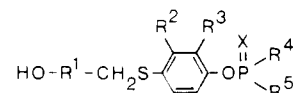
Relation between Chemical Structure and Insecticidal Activity. Previously, it was found that the biological activity of the fiber-reactive organophosphorus esters closely parallels the activity of their hydroxy precursors (Jones, 1983a,b). Therefore, for optimization of

Table V. Insecticidal Activity of Fiber-Reactive Compounds

compd no.	min concn, mg/g of wool, before and after reaction with wool to control feeding damage due to					
	<i>A. flavipes</i>		<i>T. bisselliella</i>		<i>T. translucens</i>	
	unreacted ^a	reacted ^b	unreacted	reacted	unreacted	reacted
35	0.4	0.4	0.7	0.7	1.3	1.4
36	0.7	1.3	0.8	1.3	0.5	1.2
37	0.08	0.1	0.1	0.15	0.07	0.1
38	0.08	0.09	0.3	0.4	0.5	0.5
39	0.4	0.5	0.6	0.7	1.2	1.4
40	1.0	1.7	0.9	1.4	0.7	1.7
41	0.06	0.08	0.2	0.2	0.08	0.1
42	0.08	0.1	0.3	0.3	0.6	0.7

^a Applied to wool from acetone. ^b Amount of insecticide present on the wool after application from a dye bath followed by Soxhlet extraction.

the insecticidal activity of fiber-reactive compounds based on 4-(alkylthio)phenol, a series of hydroxy esters was synthesized and evaluated. These compounds have the general formula A:



From Tables I, II, and IV the following general conclusions were drawn: (1) The largest variations in biological activity were produced by changes in the substituents (X, R⁴, and R⁵) on the phosphorus atom. (2) Phosphorothionates were more biologically active than the corresponding phosphates but less active than the isomeric phosphorothiolates. (3) Phosphorothiolothionates were only slightly less active than the corresponding phosphorothiolates. (4) Optimum insecticidal activity was obtained when R⁴ = ethoxy and R⁵ = *n*-propylmercapto. (5) Chain branching or unsaturation in R⁵ decreased insecticidal activity, especially against *Tinea translucens*. (6) The phosphonates, phosphonothionate, and phosphoramidate examined possessed poor insecticidal activity. (7) Electron-withdrawing substituents (R² and R³) in the phenyl ring had little effect on insecticidal activity. (8) Oxidation of the sulfide group to a sulfoxide group decreased the insecticidal activity slightly. (9) *T. translucens* was the most difficult insect to control with this class of compound. (10) The compounds with a secondary hydroxyl group were more active against *T. translucens* but less active against *A. flavipes* than the analogous compounds containing a primary hydroxyl group.

Fiber-Reactive Compounds. 3-(Vinylsulfonyl)propionyl and 2-bromoacryloyl esters of compounds 4, 9, 18, and 24 were prepared (Table IV) and their insecticidal activity was determined.

When these compounds were applied to the surface of the wool under conditions that did not promote reaction with the wool, the insecticidal activity of the fiber-reactive compounds (Table V), on an equimolar basis, was similar to that of the parent compounds (Table IV). However, when they were allowed to diffuse into the swollen fibers and react with the wool, by application from a boiling dye-liquor, two of the compounds (36 and 40) exhibited a marked decrease in insecticidal activity. This decrease corresponded to a marked increase in hydrolytic stability of the covalently bound compounds (Table VI). Both these effects are thought to be due to the presence of the methyl group adjacent to the carboxylic ester group which would be expected to sterically hinder the cleavage of the

Table VI. Rate of Hydrolysis of Fiber-Reactive Esters Chemically Bound to the Wool

compd no.	$t_{1/2}$, h, at 100 °C, pH 5
35	3.98
36	6.21
37	2.10
38	5.89
39	3.81
40	5.14
41	1.95
42	5.29

carboxylic ester group either enzymically by the insect or hydrolytically in the dye-liquor.

The most hydrolytically unstable compounds on the wool were the phosphorothiolates 37 and 41. The phenoxy-phosphorus bond in these compounds is much more susceptible to hydrolysis than the corresponding bond in the phosphorothionate and phosphorothiothionate esters (Eto, 1974). This means that when these compounds (37 and 41) are applied in a boiling dye bath, more must be applied to account for the hydrolytic losses. However, when compared with the other compounds, this lower hydrolytic stability was more than compensated for by the greatly increased insecticidal activity.

CONCLUSIONS

Unlike the organophosphorus esters of nitrogen heterocyclic compounds (Jones, 1983a), but similar to the esters of 4-nitrophenol (O'Loughlin, 1982) the phosphorus esters of 4-[(2-hydroxyethyl)thio]phenol displayed the greatest insecticidal activity against wool pests when a *n*-propylthio group was attached to the phosphorus atom. Structural variations in other parts of the molecule produced much smaller variations in insecticidal activity.

The hydrolytic stability of fiber-reactive esters was improved by the presence of an alkyl substituent adjacent to the carboxylic ester bond, but this substituent also reduced the accessibility of the insecticide to the target insect.

Although phosphorothiolate esters were less hydrolytically stable than the corresponding phosphorothionates

and phosphorothiothionate esters, they were more insecticidally active against wool-textile pests and therefore offer more potential as insecticides suitable for the protection of wool.

ACKNOWLEDGMENT

I thank C. R. Nunn for technical assistance.

Registry No. 1, 84009-90-5; 2, 84009-91-6; 3, 84009-92-7; 4, 70308-26-8; 5, 84009-93-8; 6, 84009-94-9; 7, 84009-95-0; 8, 84009-96-1; 9, 76788-75-5; 10, 84009-97-2; 11, 84009-98-3; 12, 77160-39-5; 13, 84009-99-4; 14, 84010-00-4; 15, 84010-01-5; 16, 84010-02-6; 17, 84010-03-7; 18, 76788-73-3; 19, 76798-60-2; 20, 84010-04-8; 21, 84010-05-9; 22, 84010-06-0; 23, 84027-30-5; 24, 84027-31-6; 25, 84010-07-1; 26, 84010-08-2; 27, 84010-09-3; 28, 84027-32-7; 29, 84010-10-6; 30, 84010-11-7; 31, 84010-12-8; 32, 84010-13-9; 33, 84010-14-0; 34, 84010-15-1; 35, 70307-89-0; 36, 84010-16-2; 37, 80241-48-1; 38, 70307-85-6; 39, 70307-82-3; 40, 84010-17-3; 41, 80241-52-7; 42, 70307-93-6; 4-[(2-hydroxyethyl)thio]phenol, 30519-04-1; 2-chloro-4-[(2-hydroxyethyl)thio]phenol, 38407-53-3; 3-chloro-4-[(2-hydroxyethyl)thio]phenol, 84010-18-4.

Supplementary Material Available: A tabulation of the ^1H NMR spectra and microanalysis data of the organophosphorus esters (11 pages). Ordering information is given on any current masthead page.

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Received for review May 3, 1982. Accepted October 18, 1982.