derivatives of methomyl. Results of those investigations are reported in the following paper (Dutton et al., 1981).

ACKNOWLEDGMENT

We acknowledge the assistance of L. H. Hope and P. A. Timmons in the biological evaluations and P. K. Brown in the toxicological investigations.

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Insecticidal Phosphorinanylaminothio Derivatives of the Carbamate Methomyl

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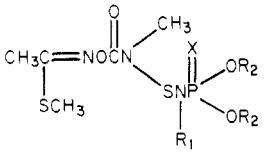
The insecticidal activities of phosphorinanylaminothio derivatives of methomyl were examined. The derivatives demonstrated activity comparable to that of methomyl in feeding tests against southern armyworm (*Spodoptera eridania*, Cramer), cabbage looper (*Trichoplusia ni*, Hubner), and tobacco budworm (*Heliothis virescens*, Fabricius) but had reduced topical and ovicidal activities against the same species. Of the compounds tested, none were phytotoxic toward cotton, eggplant, and soybean and demonstrated significantly greater residual effectiveness than did methomyl. Mammalian toxicity was shown to be substantially reduced relative to that of methomyl, and three of the compounds had acute oral LD_{50} values of over 8000 mg/kg to male rats. These compounds perhaps demonstrate the greatest selectivity yet achieved through N-substitution of pesticidal carbamates.

In the preceding paper (Dutton et al., 1981), we reported results of our investigations of phosphoramidothio derivatives (1) of methomyl. These compounds demonstrated



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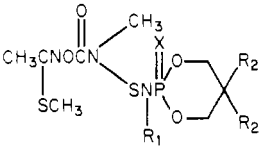

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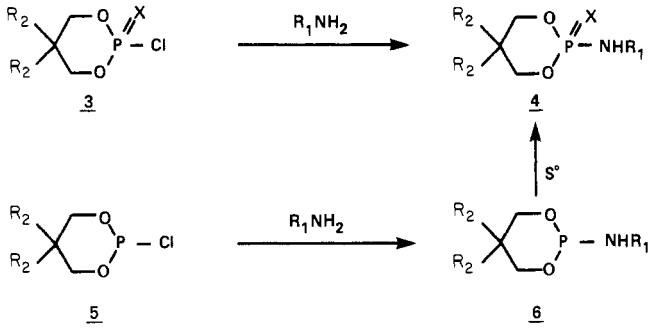
insecticidal activity toward lepidopterous larvae approximately equal to that of methomyl but showed reduced phytotoxicity, longer residual activity, and substantially reduced mammalian toxicity. As part of our continuing effort to modify carbamate insecticides having high activity but which suffer shortcomings in their ancillary properties, we have investigated the closely related phosphorinanylaminothio derivatives (2) of methomyl.

EXPERIMENTAL SECTION

Synthesis of Compounds. The phosphorinanamines 4 required for the preparation of the derivatives were obtained by reaction of a primary amine with the appropriate chlorophosphorinane 3 (Sasse, 1964), as outlined in Scheme I. In those cases where X is sulfur and the primary amine is hindered, it proved much more convenient to react the phosphorochloridite 5 with the amine (Cogne et al., 1974), followed by treatment with elemental sulfur.

Scheme I. Synthesis of Phosphorinanamines



The phosphorinanamines 4 were coupled with methomyl through the *N*-chlorothio or -bromothio intermediates 8 which were obtained by reaction of the corresponding disulfides 7 with elemental halogen (Scheme II). Although bromothio compounds and their chemistry are reported (Kuhle, 1970), this is to our knowledge the first example of their use in the preparation of *N*-thiocarbamates. In

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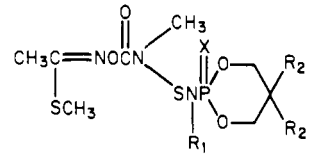
Table I. Physical Properties[a] and Method of Synthesis[b] of Phosphorinanylaminothio Carbamates



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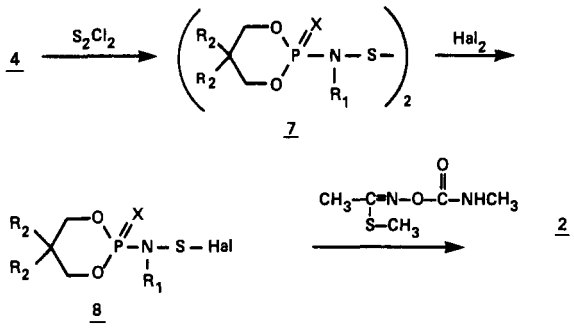
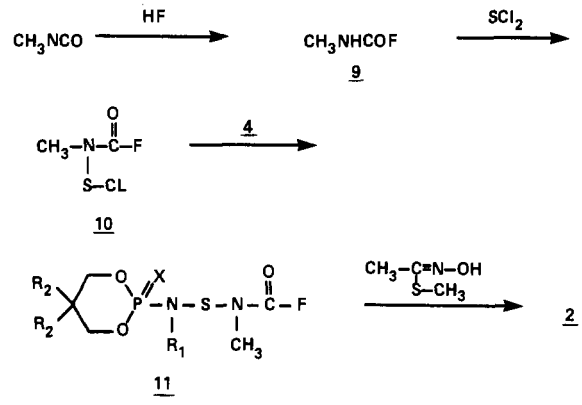
compd	R_1	R_2	X	mp, °C	method of synthesis
2a	$CH(CH_3)_2$	CH_3	S	114-115	A
2b	$C(CH_3)_3$	CH_3	S	166-168	A, B
2c	C_6H_{11}	CH_3	S	138-140 dec	A
2d	C_6H_{11}	CH_2CH_3	S	155-157	A
2e	$CH(CH_3)_2$	H	S	153-154	A, B
2f	CH_3	CH_2CH_3	S	123-125	A
2g	CH_3	H	S	93-69	A
2h	$CH(CH_3)_2$	H	O	134-135	B
2i	$C(CH_3)_3$	CH_3	O	133-134	B

[a] Satisfactory elemental analyses (±0.4%) were obtained for all compounds. [b] Method A: *N*-halothiophosphoramide intermediate. Method B: carbamoyl fluoride intermediate.

Scheme II. Synthesis of Phosphorinanylaminothio Derivatives of Methomyl: Method A



Scheme III. Synthesis of Phosphorinanylaminothio Derivatives of Methomyl: Method B



this series yields were increased 15–20% relative to those of the reaction with chlorothio intermediates. The disulfides were readily prepared by the reaction of the phosphorinanamines **4** with sulfur monochloride.

In several instances, particularly with the P=O phosphoramides, the reaction of methomyl with the halothio intermediates led to complicated mixtures from which the desired products were isolated in low yields. A route based on the carbamoyl fluoride intermediates **11** (Scheme III), analogous to that employed in the preparation of aminothio derivatives of carbofuran (Hatch, 1978), proved superior for the preparation of compounds **2b**, **2e**, **2h**, and **2i**.

Previously reported procedures (Hatch, 1978) for the preparation of *N*-methylcarbamoyl fluoride (**9**) have utilized an excess of hydrogen fluoride (HF), necessitating specialized equipment and the removal and disposal of corrosive HF. We have found that through the simple expediency of passing anhydrous HF into excess neat methyl isocyanate in normal glassware a product which can be stored in glass containers for several months without any noticeable etching is obtained in high yield. The remaining steps in the sequence are uneventful and provide the final products in modest to good overall yields. Physical data and method of synthesis for the derivatives are given in Table I.

As a typical example of the chlorothiophosphorinanamine coupling sequence (Scheme II, method A), the preparation of methyl *N*-[[[[[(5,5-dimethyl-1,3,2-dioxaphosphorinan-2-yl)(1,1-dimethylethyl)amino]thio]-methylamino]carbonyl]oxy]ethanimidothioate (**2b**, Table I) and corresponding intermediates is given.

N-(1,1-Dimethylethyl)-5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-amine (**4b**). Sulfur (3.20 g, 0.100 mol) was added in portions to a solution of *N*-(1,1-dimethylethyl)-5,5-dimethyl-1,3,2-dioxaphosphorinan-2-amine (Cogne et al., 1974) (20.5 g, 0.100 mol) in methylene chloride (75 mL) over 10 min. After the addition the mixture was stirred at room temperature for 10 min, and the solvent was removed under reduced pressure to leave the title compound (23.7 g, 100%) as a white solid, mp 128–130 °C. Recrystallization from methanol provided an analytical sample: mp 128–130 °C; NMR ($CDCl_3$) δ 0.82 (s, 3 H), 1.25 (s, 3 H), 1.39 (s, 9 H), 3.52–4.00 (m, 2 H), 4.28–4.53 (m, 2 H).

N,N'-Dithiobis-N-(1,1-dimethylethyl)-5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-amine (**7b**). The phosphorinanamine from above (11.9 g, 50.1 mmol) was suspended in acetonitrile (100 mL), and the mixture was cooled in an ice–methanol bath to −10 °C. Triethylamine (5.08 g, 50.3 mmol) was added, followed by dropwise addition of freshly distilled sulfur monochloride (3.38 g, 50.0 mmol) over 5 min. After the addition the mixture was

Table II. Synopsis of Biological Evaluations

organism or type of test	stage	principal mode of contact	method of application	time post-treatment, days, to evaluation
cabbage looper[a]	O[g]	contact	dip	3
cabbage looper	L-1[h]	feeding	leaf[l] dip	3
housefly[b]	A[i]	feeding	treated 10% sugar soln	2
southern armyworm[c]	L-3[j]	feeding	leaf[m] dip	3
tobacco budworm[d]	0	contact	dip	3
tobacco budworm	L-1	feeding	leaf[l] dip	3
tobacco budworm	L-3	feeding	topical application	3
phytotoxicity[e]	seedling[k]	contact	full coverage sprays	8[n]
cotton foliar residual/ cabbage looper	seedling/L-3	contact/feeding	plant dip	20[o]
acute oral rat[f]	190-220 g	oral	gastric intubation	7/14[p]

[a] *Trichoplusia ni.* [b] *Musca domestica.* [c] *Spodoptera eridania.* [d] *Heliothis virescens.* [e] Cotton, *Gossypium hursutum*, cv. Delta Pine 16; eggplant, *Solanum melongena*, cv. Black Beauty; soybean, *Glycine max*, cv. Amsoy 71. [f] Sprague-Dawley white rats. [g] Ova. [h] Neonate larvae. [i] Adults. [j] Third instar larvae. [k] Two or more fully expanded noncotyledonary leaves/plant. [l] Cotton. [m] Lima bean, *Phaseolus vulgaris*, cv. Henderson bush. [n] Plants evaluated for injury 8 days following the third weekly spray application. [o] Plants held 20 days posttreatment prior to evaluation of foliar toxicity to cabbage looper larvae; percent larval mortality was recorded 3 days after infestation. [p] In preliminary studies rats were evaluated for mortality after 7 days and after 14 days in refined tests.

warmed to room temperature over 20 min and then diluted with water (25 mL). The precipitate was collected and dried to give the disulfide (10.4 g, 78%) as a white solid, mp 162–164 °C. Recrystallization from acetone provided an analytical sample: mp 162–164 °C; NMR ($CDCl_3$) δ 0.85 (s, 6 H), 1.21 (s, 6 H), 1.58 (s, 18 H), 3.35–4.50 (m, 8 H).

Methyl N-[[[[[(1,1-Dimethylethyl)(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)amino]thio]methylamino]carbonyl]oxy]ethanimidothioate **(2b).** Bromine (16.0 g, 0.100 mol) was added over 5 min to a suspension of the above disulfide (53.6 g, 0.100 mol) in THF (200 mL) cooled at 0 °C. After the addition the mixture was stirred for 15 min during which time the disulfide completely dissolved to give a dark red solution. This was added dropwise over 15 min to a solution of methomyl (32.4 g, 0.200 mol), triethylamine (20.2 g, 0.200 mol), and cuprous chloride (0.35 g) in THF (300 mL) with cooling to maintain a temperature of −12 °C. After the addition the mixture was stirred at −12 °C for 2 h and then diluted with hexane (500 mL). The precipitate was collected, washed with cold 1:1 methanol–water (2 × 200 mL), and dried to give a crude product as a tan solid (67.8 g, 79%). Recrystallization from acetonitrile gave an analytical sample: mp 166–168 °C; NMR ($CDCl_3$) δ 0.88 (s, 3 H), 1.26 (s, 3 H), 1.55 (s, 9 H), 2.25 (s, 3 H), 2.35 (s, 3 H), 3.45 (s, 3 H), 3.55–4.20 (m, 4 H); IR ($CHCl_3$) 1735 cm^{-1}.

The following alternative sequence for the preparation of **2b** is typical of the carbamoyl fluoride route (Scheme III, method B).

N-Methylcarbamoyl Fluoride **(9).** Anhydrous HF (21.8 g, 1.09 mol) was bubbled slowly into methyl isocyanate (72.5 g, 1.27 mol) through a 2 mm i.d. polyethylene tube with cooling to maintain a reaction temperature of 5–10 °C. After the addition the excess methyl isocyanate was removed at 25 °C and 40–60 mmHg to leave the product as a clear colorless liquid (83.8 g, 99.7%). The material distills at 48 °C, 10 mmHg: NMR ($CDCl_3$) δ 2.87 (d, J = 4.9 Hz).

N-(Chlorothio)methylcarbamoyl Fluoride **(10).** A solution of pyridine (11.3 g, 0.143 mol) in methylene chloride (20 mL) was added over 10 min to a solution of *N*-methylcarbamoyl fluoride (10.0 g, 0.130 mol) and freshly distilled sulfur dichloride (17.4 g, 0.169 mol) in methylene chloride (50 mL) cooled to −10 °C. After the addition the mixture was warmed to room temperature and stirred for 20 h. The mixture was diluted with ether and the precipitated pyridine hydrochloride filtered under nitrogen. The filtrate was concentrated under reduced pressure with a bath temperature of less than 30 °C to give a crude product (18.3 g) as a clear yellow oil. The ^1H NMR spectrum ($CDCl_3$; δ 3.50) indicated small amounts of pyridine hydrochloride, methylcarbamoyl fluoride, and methylene chloride and a purity of 80–85%. Flash distillation (30–35 °C, 7 mmHg) gave material of 95% purity.

Methyl[[(1,1-dimethylethyl)(2-thioxo-1,3,2-dioxaphosphorinan-2-yl)amino]thio]carbamoyl Fluoride **(11b).** A solution of *N*-(1,1-dimethylethyl)-5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-amine (18.3 g, 77 mmol) and triethylamine (8.60 g, 85 mmol) in THF (50 mL) was added dropwise over 10 min to a solution of *N*-(chlorothio)-methylcarbamoyl fluoride (15.29 g, 77 mmol) in THF (50 mL) cooled to −5 °C. The mixture was stirred for 1.5 h at 0 °C and then diluted with ether (200 mL) and washed with ice water (2 × 300 mL), brine, dried over sodium sulfate, and concentrated under reduced pressure with a bath temperature of less than 30 °C. The residual yellow oil was triturated with ether–hexane to precipitate the product (10.47 g, 39%) as a tan solid. Recrystallization from ethyl acetate gave an analytical sample: mp 147–149 °C; NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.25 (s, 3 H), 1.55 (s, 9 H), 3.45 (s, 3 H), 3.60–4.20 (m, 4 H); IR (Nujol) 1818 cm^{-1}.

Although crystalline in this case, the carbamoyl fluoride intermediates were usually obtained as oils which resisted purification by normal procedures and consequently were generally used as obtained.

Preparation of **2b.** A solution of the carbamoyl fluoride **11b** from above (689 mg, 2.00 mmol), methyl *N*-hydroxyethanimidothioate (Registry No. 13749-94-5; 210 mg, 2.10 mmol), and triethylamine (217 mg, 2.14 mmol) in acetonitrile (5.00 mL) was stirred for 5 h at room temperature and then diluted with water (15 mL). The resultant precipitate was collected and dried to give 800 mg (93%) of **2b**. Recrystallization from acetonitrile gave **2b**, mp 164–167 °C.

Biological Test Methods. Except as noted below, compounds were formulated and evaluated by using procedures similar or identical with those cited in the preceding paper (Dutton et al., 1981). For reference purposes, these test methods are summarized in Table II.

Foliar feeding toxicity studies directed at cabbage looper and tobacco budworm larvae and housefly tests were conducted according to a modification of the procedures

Table III. Insecticidal Activity[a] and Mammalian Toxicity of Phosphorinanylaminothio Derivatives of Methomyl

compd	foliar feeding SAW[b]	foliar feeding CL[c]	foliar feeding TBW[d]	feeding, HF[e]	ovicidal TBW	ovicidal CL	topical, TBW	male rat (oral) LD50
2a	++++	++±±	+±−−	++±−	++−			800
2b	+++−	++±−	+±−−	+−−−	+±−	++±±	+±±−	>8000
2c	++−−	++±−	+±±−	++−−	+±−	++±−		8000
2d	±−−−	++±±	++±−	+±−−	+±−	++±−		>8000
2e	++++	++±−	+±−−	++−−	+±±	+++−	±−−−	600
2f	+++−	+++±	+±−−	+−−−				
2g	++−−	+++±	+±−−	++++				
2h	++−−	++−−	+±−−	++++			−−−−	
2i	++±−	+++±	±−±−	++++			±−−−	
methomyl	+++−	++±−	+±−−	++++	+++	++++	++±−	

[a] (+) 71–100% corrected (Abbott's formula) mortality; (±) 36–70%; (−) 0–35%. Rates: SAW, 50, 17, 5.5, and 1.8 ppm; CL and TBW (feeding), 12, 4, 1.3, and 0.4 ppm; HF, 50, 25, 12.5, and 6.2 ppm; TBW and CL (ovicidal), 100, 33, 11, and 3.7 ppm; topical, TBW, 35, 18, 9, and 4.5 μg/g. [b] Southern armyworm. [c] Cabbage looper. [d] Tobacco budworm. [e] Housefly.

of Gemrich et al. (1976). In the larval tests, cotton leaves were dipped into emulsions of the test compounds and allowed to dry, and then a single leaf was placed in a Petri dish. Forty neonate larvae were evaluated at each concentration, held at 20–22 °C, and mortality was assessed after 72 h.

For tests against houseflies, acetone solutions of the chemicals were diluted with an aqueous solution of sucrose (10%), Lignosol SFX (0.01%), and Nekal BA77 (0.01%) (Dutton et al., 1981). Ten milliliters of the desired sugar solution was added to the feeding compartment in a 120-cm^3 holding chamber. Thirty adult house flies of mixed sexes were tested at each concentration, held at 20–22 °C, and mortality was recorded after 48 h.

RESULTS AND DISCUSSION

The results of the insecticidal evaluations are summarized in Table III. Although some differences were noted in species selectivity, the compounds demonstrated high insecticidal activity, generally comparable to that of methomyl especially in feeding bioassays against leipdopterous larvae.

In contrast to the acyclic phosphoramide derivatives (Dutton et al., 1981), all compounds proved more toxic to cabbage looper than tobacco budworm in the feeding test. In this test, neonate larvae were used while in the test with the acyclic compounds third instar larvae were utilized. Since the activity in both tests parallels that of methomyl, it seems reasonable that the contrast is due to different susceptibilities of the two species at different stages of development.

Activity toward housefly was substantially reduced with the exception of compounds **2g–i**. Interestingly, the relatively high activity of the P=O compounds **2h** and **2i** stands in sharp contrast to that of the analogous P=S compounds **2e** and **2b** and derives from a minor structural difference.

The topical activities of compounds **2b**, **2e**, **2h**, and **2i** were all found to be less than that of methomyl unlike the equal or greater activity reported for the acyclic series (Dutton et al., 1981). The P=S compounds (**2h** and **2e**), however, were more active than the analogous P=O compounds (**2h** and **2i**) as was also found for the acyclic derivatives. Ovicidal activity of the derivatives tested was also less than methomyl.

No definitive structure activity correlation is apparent as was the case for the analogous acyclic derivatives. As the insecticidal evaluations did not provide a clear rationale for choosing one compound for further evaluation, we turned to a study of other biological properties.

Compounds **2b–e** were evaluated for phytotoxic properties and residual effectiveness. In the phytotoxicity test, these compounds caused no damage after three applications at 1200 ppm to cotton, eggplant, or soybeans. Under these conditions methomyl exhibited moderate to severe phytoxicity (plant injury ratings between 5 and 8, where 0 = no injury and 10 = plants dead). In the residual test these same compounds retained 59–83% of their original foliar toxicity after 20 days compared to methomyl which retained 8%. Although encouraging, the results from both tests still did not provide a clear distinction among the derivatives tested. Consequently, the mammalian safety of compounds **2a–e** was examined.

In preliminary tests, the compounds demonstrated substantially reduced oral toxicity to rats when compared to methomyl (less than $^1/_{30}$ as toxic), and surprisingly, compounds **2b–d** were on the order of $^1/_{10}$ as toxic as compounds **2a** and **2e**. Despite the large differences in oral toxicities between the compounds, all produced toxicological symptoms typical of anticholinesterase agents at elevated dosages, suggesting that the ultimate mode of intoxication for the compounds is similar, if not identical.

The comparable lepidopterous larvicidal activities of these compounds implies that regardless of the structural modifications examined, lepidopterous species tend to indiscriminantly activate the compounds to methomyl. The marked differences in mammalian toxicities between the compounds tested, however, suggest that if conversion to methomyl is responsible for inducing toxicity in rats, the rate of conversion is much more dependent on minor chemical modifications.

Compounds **2b** and **2e** were further evaluated, and the substantial difference in toxicity between sexes observed for one of the acyclic compounds (U-47319) was also found for compound **2e** (males, 1002 mg/kg; females, 427 mg/kg) and, to a lesser extent, for compound **2b** (males, 9098 mg/kg; females, 7652 mg/kg). With insecticidal activity against leipdopterous species comparable to that of methomyl and an increase in mammalian safety of more than 400-fold, compounds **2b–d** represent to our knowledge the greatest increase in selectivity yet achieved through N-substitution of carbamate insecticides.

The toxicological and insecticidal properties of compound **2b** (U-56295) prompted further evaluation of this material. Unpublished results of field trials have shown U-56295 to be a promoising candidate for the control of lepidopterous pests of agronomic and horticultural crops with substantially reduced toxicity toward beneficial arthropods.

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Pyrethroid Insecticides Derived from [1,1′-Biphenyl]-3-methanol

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The relationship of changes in southern armyworm (*Spodoptera eridania*) topical activity to variation of the physical and chemical properties of meta substituents was examined for a series of meta-monosubstituted benzyl esters of *cis,trans*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid. With the exception of substituents containing two-atom bridges between the benzyl ring and a second aromatic ring, there was a significant dependence of the activity on the oil/water partitioning property (π) of the substituent. The phenyl substituent fits this relationship closely, indicating that it is not necessary to have a bridging group between the aromatic rings of 3-substituted benzyl alcohols in order for their esters to display high pyrethroid-like activity. ([1,1′-Biphenyl]-3-yl)methyl *cis,trans*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate was found to have initial and residual activity paralleling that of permethrin against a number of insects.

The alcohol portion of most active pyrethroids contains two centers of unsaturation separated by a bridging atom. In allethrin and resmethrin this structural feature is represented by the carbon atom of the methylene groups while in permethrin the bridging atom is oxygen. Qualitative discussions of structure–activity relationships of pyrethroids have generally pointed to this feature as a requirement for good insecticidal activity. At one time it was suggested that the bridging group may actually perform a function at the active site (Elliott, 1969), while more recently it has been suggested that the lack of coplanarity between the centers of unsaturation, that results from the presence of the bridging group, provides optimum fit at the active site (Elliott et al., 1974).

We wish to report a quantitative study of the structure–activity relationships of meta-monosubstituted benzyl esters of *cis,trans*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid (DVA) conducted with the intent of either expressing the requirements for this bridging group quantitatively or finding alternate requirements for activity for such esters. Additionally, we wish to report a new series of insecticidal pyrethroid esters of [1,1′-biphenyl]-3-methanol that were prepared as part of this study.

MATERIALS AND METHODS

Chemicals. Esters and α-cyano esters of all pyrethroid acids cited were prepared by one of the three methods described below. Acceptable elemental and spectroscopic data were obtained for all novel compounds.

([1,1′-Biphenyl]-3-yl)methyl cis,trans-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate. (1) Method A. A solution of [1,1′-biphenyl]-3-methanol (0.025 mol), prepared by the method of Hammond and Reeder (1958), DVA chloride (cis/trans = 40:60) (0.025 mol), and pyridine (0.025 mol) in methylene chloride was stirred at room temperature for 16 h. The mixture was taken up in water and extracted with chloroform. The chloroform extracts were washed sequentially with 2 N HCl, saturated salt solution, and 2 N NaOH. The dried solution ($MgSO_4$) was concentrated and short path distilled at 130 °C/0.25 mmHg to give an 82% yield of oily product: NMR ($CDCl_3$) δ 1.15 (s), 1.22 (s), 1.26 (s), 1.30 (s), 1.62–2.41 (m), 5.19 (s), 5.63 (d), 6.34 (dd), 7.20–7.77 (m). Anal. Calcd for $C_{21}H_{20}Cl_2O_2$: C, 67.21; H, 5.37. Found: C, 67.39; H, 5.66.

(2) *Method B.* To an aqueous solution of potassium hydroxide (0.032 mol) was added *cis,trans*-DVA (cis/trans = 40:60) (0.032 mol). When all the acid had dissolved, 100 mL of heptane was added and the water removed by distillation. The dried mixture was cooled to 60 °C, and an acetonitrile solution of 3-(bromomethyl)-1,1′-biphenyl (0.032 mol), prepared by the method of Grovenstein and Wentworth (1967), and 0.1 g of 1,4-diazobicyclo[2.2.2]octane was added. The mixture was refluxed for 5.5 h and worked up by a procedure similar to that in method A.

([1,1′-Biphenyl]-3-yl)cyanomethyl cis,trans-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate. A tetrahydrofuran–water solution of the cyanohydrin of [1,1′-biphenyl]-3-carboxaldehyde (0.013 mol), which was prepared from 3-(bromomethyl)-1,1′-biphenyl by the Sommelet procedure, was combined with *cis,trans*-DVA chloride. The mixture was stirred for 16 h at room temperature and then diluted with water. The organic layer, combined with a chloroform extract of the aqueous layer, was washed sequentially with saturated $NaHCO_3$, saturated NaCl, saturated $Na_2S_2O_3$, and saturated NaCl solutions and dried ($MgSO_4$), and the solvent was removed. Silica gel chromatography (20% hexane–$CHCl_3$) gave 3.3 g or 63% of oily product: NMR ($CDCl_3$) δ 1.17 (s), 1.22 (s), 1.32 (s), 1.35 (s), 1.65–2.45 (m), 5.63 (dd), 6.23 (d), 6.47 (s), 6.50 (s), 7.27–7.77 (m) (cis/trans = 36:64). Anal. Calcd for $C_{22}H_{19}Cl_2NO_2$: C, 66.01; H, 4.78. Found: C, 66.41; H, 5.22.

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