Also apparently not essential to activity is the unsaturation of the exocyclic carbon–nitrogen double bond, i.e., reduced thiosemicarbazone **18**, *N,N*-dimethyl-2-[1-(2-pyridinyl)-ethyl]hydrazinecarbothioamide (**60**), and reduced **23**, 2-[1-(2-pyridinyl)ethyl]hydrazide of 1-pyrrolidinecarbothioic acid (**61**), were both active at the minimal dose of 0.1 μg/nymph.

In summary, we have identified several critical features of thiosemicarbazone derivatives that influence biological activity. Also, we report six additional analogues that elicit appreciable ecdysis-inhibiting effects in *O. fasciatus* when topically applied in doses as low as 0.05–1.0 μg/nymph. This work may serve as a useful guide for the synthesis of additional candidate thiosemicarbazone insect growth regulators.

**Registry No.** **1**, 81742-04-3; **2**, 85748-35-2; **3**, 85748-36-3; **4**, 85748-37-4; **5**, 60273-81-6; **6**, 85748-38-5; **7**, 6839-90-3; **8**, 75013-64-8; **9**, 32646-35-8; **10**, 75013-65-9; **11**, 32646-25-6; **12**, 75013-66-0; **13**, 75013-69-3; **14**, 70618-53-0; **15**, 63698-06-6; **16**, 70618-31-4; **17**, 70618-03-0; **18**, 71555-14-1; **19**, 71555-17-4; **20**, 71555-19-6; **21**, 71555-21-0; **22**, 71592-42-2; **23**, 71555-26-5; **24**, 71555-29-8; **25**, 71555-39-0; **26**, 71555-28-7; **27**, 16552-99-1; **28**, 85748-39-6; **29**, 85748-40-9; **30**, 85748-41-0; **31**, 85748-42-1; **32**, 85748-43-2; **33**, 85748-44-3; **34**, 75013-88-6; **35**, 85748-45-4; **36**, 14534-93-1; **37**, 85748-46-5; **38**, 85748-47-6; **39**, 85748-48-7; **40**, 85748-49-8; **41**, 85762-03-4; **42**, 85748-50-1; **43**, 85748-51-2; **44**, 85748-52-3; **45**, 85748-53-4; **46**, 85748-54-5; **47**, 85748-55-6; **48**, 85748-56-7; **49**, 85748-57-8; **50**, 85748-34-1; **51**, 6499-14-5; **52**, 85748-58-9; **53**, 2652-62-2; **54**, 21198-45-8; **55**, 85748-59-0; **56**, 85748-60-3; **57**, 85748-61-4; **58**, 35578-80-4; **59**, 35578-82-6; **60**, 83476-77-1; **61**, 83476-78-2; II, 5397-03-5; VI, 1192-63-8; VII, 85748-62-5; VIII, 85748-63-6; pyrrolidine, 123-75-1; 1-pyrrolidinethiocarbonyl chloride, 19009-42-8; dimethylthiocarbamoyl chloride, 16420-13-6; 1-acetylisoquinoline, 58022-21-2; 2-acetylpyridine, 1122-62-9; ethyl hydrazinecarboxylate, 4114-31-2; *tert*-butyl hydrazinecarboxylate, 870-46-2; isopropyl isocyanate, 1795-48-8; methylhydrazine, 60-34-4.

LITERATURE CITED

Jensen, K. A.; Anthoni, U.; Kagi, B.; Larsen, C.; Pedersen, C. T. *Acta Chem. Scand.* **1968**, *22*, 1–50.
Jensen, K. A.; Pedersen, C. *Acta Chem. Scand.* **1961**, *15*, 991–1002.
Kelly, T. J.; Redfern, R. E.; DeMilo, A. B.; Bořkovec, A. B. *Pestic. Biochem. Physiol.* **1982**, *17*, 35–41.
Kelly, T. J.; Woods, C. W.; Redfern, R. E.; Bořkovec, A. B. *J. Exp. Zool.* **1981**, *218*, 127–132.
Klayman, D. L.; Bartosevich, J. F.; Griffin, T. S.; Mason, C. J.; Scovill, J. P. *J. Agric. Food Chem.* **1979a**, *22*, 855–862.
Klayman, D. L.; Scovill, J. P.; Bartosevich, J. F.; Bruce, J. *J. Med. Chem.* **1983**, *26*, 35–39.
Klayman, D. L.; Scovill, J. P.; Bartosevich, J. F.; Mason, C. J. *J. Agric. Food Chem.* **1979b**, *22*, 1367–1373.
Mitsui, T.; Nobusawa, C.; Fukami, J.; Collins, J.; Riddiford, L. *J. Pestic. Sci.* **1980**, *5*, 335–341.
Nardi, D.; Massarani, E.; Tajana, A.; Degen, L.; Magestretti, M. J. *J. Med. Chem.* **1967**, *10*, 530–533.
Ohme, V.; Preuschhof, H. *J. Prakt. Chem.* **1971**, *313*, 626–635.
Redfern, R. E.; Kelly, T. J.; Bořkovec, A. B.; Hayes, D. K. *Pestic. Biochem. Physiol.* **1982**, *18*, 351–356.
Redfern, R. E.; Kelly, T. J.; Hayes, D. K. In "Juvenile Hormone Biochemistry"; Pratt, G. E.; Brooks, G. T., Eds.; Elsevier/North-Holland Biomedical Press: Amsterdam, 1981; pp 415–419.
Ried, W.; Hillebrand, H.; Oertel, G. *Justus Liebigs Ann. Chem.* **1954**, *590*, 123–128.
Sláma, K.; Romaňuk, M.; Šorm, F. "Insect Hormones and Bioanalogues"; Springer-Verlag: New York, 1974; pp 217–274.
Turner, D. L. *J. Am. Chem. Soc.* **1954**, *76*, 5175–5177.
Wibaut, J. P.; DeJonge, A. P.; van der Voort, H. G. P.; Otto, P. P. H. L. *Recl. Trav. Chim. Pays-Bas* **1951**, *70*, 1054–1066.

Received for review December 3, 1982. Accepted March 28, 1983. Mention of proprietary products does not constitute an endorsement by the U.S. Department of Agriculture.

# Pyrethroid Insecticides Derived from [1,1′-Biphenyl]-3-methanol. 2. Heteroaromatic Analogues

Ernest L. Plummer

The *cis*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid (DVA) esters of seven heterocyclic analogues of [1,1′-biphenyl]-3-methanol have been prepared. Activities for topical application against three insect species, southern armyworm, Mexican bean beetle, and milkweed bug, have been determined. The results of quantitative structure–activity studies confirm our earlier findings that for meta-monosubstituted benzyl esters of DVA the variance in southern armyworm response is correlated with the substituent lipophilicity. This provides further evidence that good activity can be obtained without a bridging atom for aromatic substituents of meta-substituted benzyl alcohols.

A common feature in most active pyrethroid esters is an alcohol portion that contains two centers of unsaturation separated by a bridging atom. Qualitative discussions of structure–activity relationships of pyrethroids have generally pointed to this feature as a requirement for good insecticidal activity (Elliott, 1969; Elliott et al., 1974). Recently a series of pyrethroid esters have been prepared from [1,1′-biphenyl]-3-methanol (Plummer and Pincus, 1981). These esters were used to demonstrate that good insecticidal activity can be obtained when the alcohol has two centers of unsaturation even if it lacks an atom bridging these centers.

We now wish to report an extention of this study in which the second center of unsaturation in a series of meta-monosubstituted benzyl esters is a heteroaromatic ring. In addition, we present quantitative structure–activity relationship (QSAR) data relating to our earlier contention that the variance in southern armyworm re-

FMC Corporation, Agricultural Chemical Group, Princeton, New Jersey 08540.

0021-8561/83/1431-0718$01.50/0 

Table I. Meta-Monosubstituted Benzyl Esters of *cis,trans*-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic Acid (Excluding the Heteroaromatic Substituent)

| | |
|---|---|
| 1, $OC_6H_5$ [a] | 11, Cl |
| 2, $C_6H_5$ [a] | 12, $NO_2$ |
| 3, $CH_2C_6H_5$ [a] | 13, $OCH_3$ |
| 4, I[a] | 14, $CH_3$ [a] |
| 5, $OCH_2C_6H_5$ | 15, F |
| 6, $CF_3$ [a] | 16, $CO_2CH_3$ |
| 7, $CH_2CH_2C_6H_5$ | 17, $C{\equiv}CC_6H_5$ |
| 8, $CH{=}CHC_6H_5$ | 18, $NHCOCH_3$ |
| 9, H | 19, $CH(CH_3)_2$ |
| 10, Br[a] | 20, $C{=}O(C_6H_5)$ [b] |

[a] Cis isomers also included in the study. [b] Only the cis isomer included in the study.

sponse for a series of meta-monosubstituted benzyl esters (Table I) is reflected in differences in the lipophilicity of the meta substituent.

## MATERIALS AND METHODS

**Chemicals.** *Ethyl 3-(1H-Pyrrol-1-yl)benzoate.* Following the method of Elming and Clauson-Kaas (1952) 2,5-dimethoxytetrahydrofuran (0.15 mol) was added to a solution of ethyl 3-aminobenzoate (0.15 mol) in glacial acetic acid. The red solution was refluxed for 1.5 h, the acetic acid removed in vacuo, and the black residue distilled (145–143 °C/2 mmHg) to give a clear oil (25.4 g, 75%) that solidified on standing: mp 62–64 °C; NMR ($CDCl_3$) $\delta$ 1.38 (3 H, t), 4.40 (2 H, q), 6.35 (2 H, d), 7.12 (2 H, d), 7.42–8.07 (4 H, m). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.99; H, 6.20.

*3-(1H-Pyrrol-1-yl)benzenemethanol.* A solution of ethyl 3-(1*H*-pyrrol-1-yl)benzoate (0.11) in diethyl ether was added to a suspension of lithium aluminum hydride (0.13 mol) in diethyl ether. After a 2.5-h reflux the mixture was stirred at room temperature for 16 h. The reaction mixture was treated with 50:50 (v/v) water–tetrahydrofuran and extracted with diethyl ether. The organic layer was dried ($MgSO_4$) and the solvent removed to give a solid product (89%): mp 67–69 °C; NMR ($CDCl_3$) $\delta$ 2.73 (1 H, br s), 4.60 (2 H, s), 6.30 (2 H, t), 7.03 (2 H, t), 6.93–7.33 (4 H, m). Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40. Found: C, 76.56; H, 6.12.

*3-(1H-Pyrrol-1-yl)phenylmethyl cis-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate (Esterification Method A).* To a solution of 3-(1*H*-pyrrol-1-yl)-phenylmethanol (0.03 mol) and pyridine (0.06 mol) in toluene was added 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (DVA chloride). The mixture was refluxed 2 h and poured into water and the organic layer withdrawn. The aqueous layer was extracted with toluene, and the toluene layers were combined and washed successively with 5% aqueous hydrochloric acid, 10% aqueous sodium carbonate, and a saturated salt solution. The organic layer was dried ($MgSO_4$) and the solvent evaporated. Silica gel chromatography (1:1 chloroform–hexane) gave an oil product (84%): NMR ($CDCl_3$) $\delta$ 1.30 (6 H, s), 1.80–2.22 (2 H, m), 5.15 (2 H, s), 6.27 (1 H, dd), 6.33 (2 H, t), 7.07 (2 H, t), 7.17–7.48 (4 H, m). Anal. Calcd for $C_{19}H_{19}Cl_2NO_2$: C, 62.64; H, 5.26. Found: C, 62.45; H, 5.56.

*2-(3-Methylphenyl)thiophene (diazotization method A)* was prepared by the method of Gomberg and Bachmann (1924). Thus, *m*-toluidine (1.0 mol) was treated sequentially with concentrated hydrochloric acid (185 mL) and sodium nitrite (1.1 mol) at 0 °C. This mixture was added to thiophene (500 g) and 40% sodium hydroxide (275 mL) added. After 21 h at 20 °C the mixture was extracted with toluene. The combined organic layers were washed with saturated brine and dried ($MgSO_4$) and the solvent removed in vacuo. The residue was short path distilled (90–108 °C/0.35 mmHg) and then chromatographed on silica gel (hexane): yield = 6%; NMR ($CDCl_3$) $\delta$ 2.35 (3 H, S), 6.85–7.53 (7 H, m).

*2-[3-(Bromomethyl)phenyl]thiophene.* To a refluxing solution of 3-(3-methylphenyl)thiophene (0.05 mol) and benzoyl peroxide (0.5 g) in carbon tetrachloride was added a mixture of benzoyl peroxide (0.5 g) and *N*-bromosuccinimide (0.06 mol). After 2.5 h, the succinimide was filtered off and the carbon tetrachloride washed with saturated brine, dried ($MgSO_4$), and evaporated in vacuo to give an oil which was short path distilled (95–150 °C/0.1 mmHg): yield = 29%; NMR ($CDCl_3$) $\delta$ 4.42 (2 H, s), 6.85–7.80 (7 H, m).

*3-(2-Thienyl)phenylmethyl cis-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate (Esterification Method B).* A mixture of *cis,trans*-DVA (0.016 mol) and potassium hydroxide (0.016 mol) in water was stirred until the solution was complete. Heptane was added and the water removed by azeotropic distillation. Acetonitrile, 2-[3-(bromomethyl)phenyl]thiophene (0.016 mol), and 1,4-diazobicyclo[2.2.2]octane (0.1 g) were added, and the mixture was heated to reflux for 1.5 h. The reaction product was poured into saturated brine and the organic layer was separated. The aqueous layer was extracted with heptane. The heptane solution was dried ($MgSO_4$) and the solvent removed in vacuo. The oily residue was short path distilled (165 °C/0.1 mmHg) and the distillate chromatographed on silica gel to give a cis,trans product. Anal. Calcd for $C_{19}H_{18}Cl_2O_2S$: C, 59.85; H, 4.75. Found: C, 59.68; H, 4.90. Fractions of pure cis were combined: yield = 23%; NMR ($CDCl_3$) $\delta$ 1.25 (6 H, d), 1.80–2.32 (2 H, m), 5.20 (2 H, s), 6.33 (1 H, dd), 7.02–7.75 (7 H, m).

*2-(3-Bromophenyl)furan (Diazotization Method B).* Using the method of Cadogan (1962), a solution of 3-bromoaniline (0.29 mol) in furan (250 mL) at 0 °C was treated with isoamyl nitrite (0.58 mol) over 0.5 h. The mixture was heated to reflux for 16 h. The product mixture was taken up in saturated brine and extracted with diethyl ether. The combined organics were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on Florisil (9:1 hexane–toluene) and short path distilled (98–105 °C/0.1 mmHg): yield = 51%; NMR ($CDCl_3$) $\delta$ 6.40–6.72 (2 H, m), 7.00–7.90 (5 H, m). Anal. Calcd for $C_{10}H_7BrO$: C, 53.84; H, 3.16. Found: C, 53.67; H, 3.45.

*3-(2-Furanyl)benzaldehyde.* A solution of 2-(3-bromophenyl)furan (0.07 mol) in diethyl ether was cooled to −78 °C. A hexane solution of *n*-butyl lithium (0.07 mol) was added. This solution was added to a solution of dimethyl formamide, in diethyl ether–THF at −78 °C. The mixture was stirred for 2 h at 20 °C and then poured into saturated brine. The aqueous mixture was extracted with diethyl ether. The combined organics were dried ($MgSO_4$) and the solvent was removed in vacuo. The aldehyde was isolated as a bisulfite addition product and after base treatment ($NaHCO_3$) was short path distilled (83 °C/0.1 mmHg): yield = 26%; NMR ($CDCl_3$) $\delta$ 6.33–6.80 (2 H, m), 7.20–8.20 (5 H, m), 10.00 (1 H, s).

*3-(2-Furanyl)benzenemethanol.* A solution of 3-(2-furanyl)benzaldehyde (0.02 mol) in absolute ethanol was treated with sodium borohydride (0.02 mol) at 20 °C for 16 h. The solvent was removed in vacuo. The residue was taken up in saturated brine and the aqueous mixture extracted with methylene chloride. The organic solution was dried ($MgSO_4$) and the solvent removed in vacuo to give a product: yield = 100%; NMR ($CDCl_3$) $\delta$ 2.40 (1 H, br

Table II. Substituted Parameters for Meta-Heteroaromatic-Substituted Benzyl Esters of *cis*-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic Acid

| substituent | log [1/(*RP*)] | $\pi$ | $\sigma_m$ | *F* | *R* | MR | *L* | $B_1$ | $B_4$ |
|---|---|---|---|---|---|---|---|---|---|
| 2-thienyl | 0.48 | 1.61 | 0.09 | 0.10 | 0.01 | 24.04 | 5.97 | 1.65 | 3.16 |
| 1-pyrrolyl | 1.14 | 0.95 | 0.47 | 0.49 | −0.03 | 22.57 | | | |
| 2-furanyl | 1.27 | 1.36 | 0.06 | 0.12 | −0.02 | 17.88 | | | |
| 2-pyridinyl | 1.51 | 0.50 | | 0.47 | −0.06 | 23.03 | | | |
| 4-pyridinyl | NSA | 0.32 | | | | 23.03 | | | |

s), 4.60 (2 H, s), 6.33–6.68 (2 H, m), 7.00–7.65 (5 H, m).

*3-(2-Furanyl)phenylmethyl cis-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxyate.* By use of esterification method A 3-(2-furanyl)benzenemethanol (0.01 mol) was treated with *cis*-DVA chloride (0.01 mol) to give a product: yield = 98%; NMR ($CDCl_3$) $\delta$ 1.25 (6 H, s), 1.73–2.25 (2 H, m), 5.18 (2 H, s), 6.30 (1 H, dd), 6.40–6.75 (2 H, m), 7.20–7.78 (5 H, m). Anal. Calcd for $C_{19}H_{18}Cl_2O$: C, 62.48; H, 4.96. Found: C, 61.29; H, 4.95.

*2-(3-Bromophenyl)pyridine, 3-(3-Bromophenyl)-pyridine, and 4-(3-Bromophenyl)pyridine.* By use of diazotization method B 3-bromoaniline (0.24 mol) was treated with isoamyl nitrite (0.58 mol) in pyridine (250 mL). The product was isolated as an oily residue and subjected to chromatograpy on silica gel (toluene). The first material off the column was 2-(3-bromophenyl)-pyridine: yield = 14.4 g; NMR ($CDCl_3$) $\delta$ 6.80–8.05 (7 H, m), 8.17–8.22 (1 H, m).

Short path distillation (99 °C/0.1 mmHg) of the remaining product gave a mixture of 3-(3-bromophenyl)-pyridine and 4-(3-bromophenyl)pyridine: yield = 6.0 g.

*3-(2-Pyridinyl)benzaldehyde.* By use of the same procedure as used for the preparation of 3-(2-furanyl)benzaldehyde, 2-(3-bromophenyl)pyridine (0.5 mol) gave a product: yield = 19%; NMR ($CDCl_3$) $\delta$ 7.0–8.8 (8 H, m), 10.00 (1 H, s).

*3-(2-Pyridinyl)benzenemethanol.* By use of a procedure similar to that used for the preparation of 3-(2-furanyl)-benzenemethanol, 3-(2-pyridinyl)benzaldehyde (0.01 mol) gave a product: yield = 94%; NMR ($CDCl_3$) $\delta$ 4.0 (1 H, br s), 4.64 (2 H, s), 7.0–8.0 (7 H, m), 8.35–8.50 (1 H, m).

*3-(2-Pyridinyl)phenylmethyl cis-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate* was prepared by general esterification method A from 3-(2-pyridinyl)benzenemethanol (0.01 mol): yield = 56%; NMR ($CDCl_3$) $\delta$ 1.23 (6 H, s), 1.80–2.20 (2 H, m), 5.20 (2 H, s), 6.32 (1 H, dd), 7.05–8.05 (7 H, m), 8.45–8.60 (1 H, m). Anal. Calcd for $C_{20}H_{19}Cl_2NO_2$: C, 63.84; H, 5.09. Found: C, 64.02; H, 5.64.

*3-(3-Pyridinyl)benzaldehyde and 3-(4-Pyridinyl)benzaldehyde.* By use of the same procedure as for 3-(2-furanyl)benzaldehyde, a mixture of 3-(3-bromophenyl)-pyridine and 4-(3-bromophenyl)pyridine (0.02 mol) gave a mixture of aldehydes that was not separated but taken directly to the next step: yield = 58%.

*3-(3-Pyridinyl)benzenemethanol and 3-(4-Pyridinyl)-benzenemethanol.* By use of the same procedure as for 3-(2-furanyl)benzenemethanol, the mixture of aldehydes was reduced with sodium borohydride. This mixture of alcohols was subjected to medium-pressure chromatography on silica gel (EtOAc) to give 3-(3-pyridinyl)benzenemethanol (0.7 g): NMR ($CDCl_3$) $\delta$ 3.65 (1 H, br s), 4.80 (2 H, s), 7.35–7.70 (6 H, m), 8.40–8.60 (2 H, m). 3-(4-Pyridinyl)benzenemethanol (1.3 g): NMR ($CDCl_3$) 3.38 (1 H, br s), 4.78 (2 H, s), 7.20–8.00 (6 H, m), 8.40–8.78 (2 H, m).

*3-(3-Pyridinyl)phenylmethyl cis-3-(2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.* By use of general esterification method A 3-(3-pyridinyl)-benzenemethanol (0.004 mol) gave a 50% yield of product: NMR ($CDCl_3$) $\delta$ 1.28 (6 H, s), 1.73–2.35 (2 H, m), 5.20 (2 H, s), 6.30 (1 H, dd), 7.35–7.70 (6 H, m), 8.40–8.65 (2 H, m).

*3-(4-Pyridinyl)phenylmethyl cis-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.* By use of general esterification method A 3-(4-pyridinyl)-benzenemethanol (0.004 mol) gave a 40% yield of product: NMR ($CDCl_3$) $\delta$ 1.28 (6 H, s), 1.72–2.32 (2 H, m), 5.20 (2 H, s), 6.30 (1 H, dd), 7.22–8.02 (6 H, m), 8.40–8.80 (2 H, m). Anal. Calcd for $C_{20}H_{19}Cl_2NO_2$: C, 63.84; H, 5.09. Found: C, 63.64; H, 5.60.

**Biological Studies.** All biological tests were conducted as previously reported (Plummer and Pincus, 1981).

**Structure–Activity Studies.** Parameters for structure–activity studies were obtained as previously described (Plummer and Pincus, 1981). The values for heteroaromatic substituents used for multiple linear regression analysis are shown in Table II. Values used for the other substituent have been presented earlier (Plummer and Pincus, 1981).

## RESULTS AND DISCUSSION

In our previous study of a series of meta-monosubstituted benzyl esters of *cis,trans*-DVA (Plummer and Pincus, 1981), we found a linear relationship between the substituent lipophilicity, as expressed by the hydrophobic substituent constant $\pi$, and topical SAW activity, as expressed by the logarithm of the inverse of the potency relative to permethrin. We concluded that a bridging atom was not necessary for good activity and that other aromatic substituents lacking a bridging atom should follow the same relationship of lipophilicity to SAW activity.

To test this concept, we prepared the six meta-heteroaromatic-substituted benzyl esters of *cis*-DVA listed in Table III. This table also reports the results to topical evaluation of these compounds against SAW. Four compounds were sufficiently active to be meaningfully studied by regression analysis.

When the evaluation data from the four heteroaromatic substituents are combined with the earlier data set, an equation (eq 1) that is essentially the same as for the smaller data set is generated.

$$\log [1/(RP)] = -1.08\pi - 0.16(\text{cis}) + 2.6 \quad (1)$$

$$n = 25 \quad r = 0.904 \quad s = 0.407 \quad F = 49.3$$

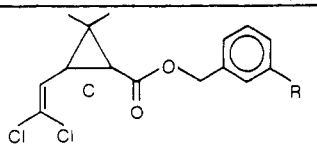
Equation 3 is expressed graphically in Figure 1. The earlier substituents left a gap between substituent 4 (I) and substituent 3 ($CH_2C_6H_5$) of nearly 1.00$\pi$ unit. The addition of the heteroaromatic substituents clearly bridges this gap.

In our earlier report we showed that the SAW response was also correlated with the molar refractivity, MR, of the meta substituent. When the heteroaromatic substituents are added, the same relationship is found. In fact, there is little difference in the quality of eq 1 and 2, a result that

$$\log [1/(RP)] = -0.08\text{MR} - 0.05(\text{cis}) + 2.68 \quad (2)$$

$$n = 25 \quad r = 0.907 \quad s = 0.402 \quad F = 50.9$$

Table III



| R | Topical Relative Potency (Permethrin = 1.0) | | |
|---|---|---|---|
| | SAW | MBB | MWB |
|  | 0.69 | 0.95 | 1.25 |
|  | 0.33 | 0.04 | 0.50 |
|  | 0.07 | 0.05 | 0.64 |
|  | 0.05 | NSA | NSA |
|  | 0.03 | NSA | NSA |
|  | NSA | NSA | 0.23 |
|  | NSA | NSA | NSA |

NSA = Not Sufficiently Active; i.e., $LD_{50}$ 5000 ppm.

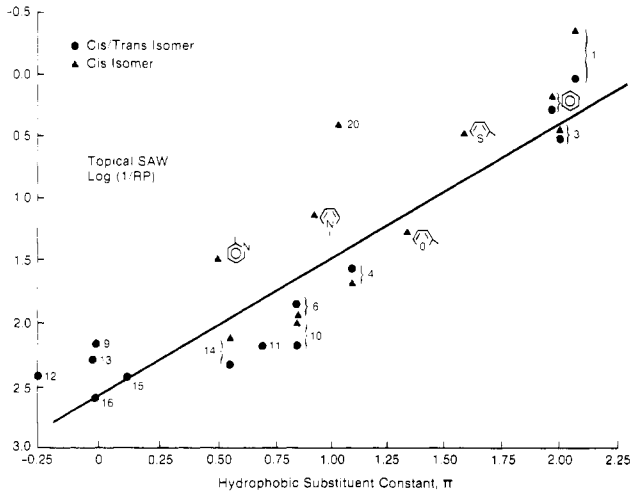



**Figure 1.** Relationship of meta-monosubstituted hydrophobic substituent constant ($\pi$) to southern armyworm biological response [log [1/(*RP*)]].

is not surprising since $\pi$ and MR are highly correlated ($r$ = 0.790). As in our earlier report no other parameter or combination of parameters explained more of the biological variation.

With the exception of the 2-furanyl-substituted ester, the compounds containing aromatic substituents are generally more active than predicted by eq 1 and 2. This may reflect an improved binding at the active site for aromatic substituents. Two substituents, 3-pyridinyl and 4-pyridinyl, produced benzyl esters of very low activity. Clearly the dipole moment changes orientation in the three pyridine isomers. Again, differences in active site binding may explain these results; however, no specific evidence was found for systematic variance of the activity with changes in any of the electronic parameters used.

In Table III, the results of topical evaluation against two other insect species is reported. As was the case with other meta-substituted benzyl esters of DVA, activity against SAW for heteroaromatic substituted esters does not necessarily correlate with activity against other species. Only the most active esters give good correlation with other species.

## CONCLUSIONS

Inclusion of four new heteroaromatic substituents with a series of meta-monosubstituted benzyl esters of DVA confirms our earlier observation that the variance in southern armyworm response is partly explained by changes in the lipophilicity or the molar refractivity of the substituent. The finding that aromatic substituents are, in general, more active than nonaromatic substituents of equivalent $\pi$ suggests that specific active site binding may be involved.

Regardless of the mode of binding, this new data confirm our earlier conclusions that good activity can be obtained when a meta substituent has two centers of unsaturation even if it lacks an atom bridging these centers.

## ACKNOWLEDGMENT

I thank David E. Seelye for his assistance in compound synthesis and John H. Leigh for his assistance in conducting topical evaluations.

**Registry No.** 2,5-Dimethoxytetrahydrofuran, 696-59-3; ethyl 3-aminobenzoate, 582-33-2; ethyl 3-(1*H*-pyrrol-1-yl)benzoate, 83140-93-6; *cis*-DVA chloride, 68539-75-3; 3-(1*H*-pyrrol-1-yl)-phenylmethanol, 83140-94-7; 2-(3-methylphenyl)thiophene, 85553-43-1; 2-[3-(bromomethyl)phenyl]thiophene, 85553-44-2; 3-(1*H*-pyrrol-1-yl)phenylmethyl *cis*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 83141-14-4; 3-(2-thienyl)-phenylmethyl *cis*-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 85553-45-3; 3-(2-furanyl)phenylmethyl *cis*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 85553-46-4; 3-(2-pyridinyl)phenylmethyl *cis*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 85553-47-5; 3-(3-pyridinyl)phenylmethyl *cis*-3-(2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 85553-48-6; 3-(4-pyridinyl)phenylmethyl *cis*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 85553-49-7; *cis*-DVA, 59042-49-8; 3-(2-thienyl)phenylmethyl *trans*-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, 85553-50-0; 3-bromoaniline, 591-19-5; isoamyl nitrite, 110-46-3; 2-(3-bromophenyl)furan, 85553-51-1; 3-(2-furanyl)benzaldehyde, 85553-52-2; *trans*-DVA chloride, 60254-21-9; 2-(3-bromophenyl)pyridine, 4373-60-8; 3-(3-bromophenyl)pyridine, 4422-32-6; 4-(3-bromophenyl)pyridine, 4373-72-2; 3-(2-pyridinyl)benzaldehyde, 85553-53-3; 3-(3-pyridinyl)benzenemethanol, 85553-54-4; 3-(4-pyridinyl)benzenemethanol, 85553-55-5; *trans*-DVA, 59042-50-1.

## LITERATURE CITED

Cadogan, J. I. G. *J. Chem. Soc.* **1962**, 4257.
Elming, N.; Clauson-Kaas, N. *Acta Chem. Scand.* **1952**, *6*, 867.
Elliott, M. *Chem. Ind. (London)* **1969**, 776.
Elliott, M.; Farnham, A. W.; Janes, N. F.; Needham, P. H. Pulman, D. "Mechanism of Pesticide Action"; American Chemical Society: Washington, DC, 1974; ACS Symp. Ser. No. 2, pp 80–91.
Gomberg, M.; Bachmann, W. E. *J. Am. Chem. Soc.* **1924**, *46*, 2339.
Plummer, E. L.; Pincus, D. S. *J. Agric. Food Chem.* **1981**, *29*, 1118.

Received for review March 15, 1982. Revised manuscript received October 18, 1982. Accepted March 14, 1983. For part 1, see Plummer and Pincus (1981).