Pestic. Sci. 1995, **44**, 261–268

The Pyrethrins and Related Compounds. Part XXXVIII*—Optimisation of Insecticidal Activity in 3-[(Alkoxyimino)methyl]-4-fluorobenzyl Esters

David G. Beddie, Andrew W. Farnham & Bhupinder P. S. Khambay‡

Department of Biological & Ecological Chemistry, Institute of Arable Crops Research, Rothamsted Experimental Station, Harpenden, Herts AL5 2JQ, UK

(Received 10 February 1994; revised version received 17 October 1994; accepted 23 February 1995)

Abstract: Optimisation of activity in 3-[(alkoxyimino)methylbenzyl] esters has been investigated by introducing an α-cyano group and a fluorine atom in position 4 of the benzylic moiety in conjunction with varying the length and nature of the side chain. Of the five side-chain variations investigated, the 3-methoxyiminomethyl was more effective than others. Introduction of fluorine in position 4 of the benzylic moiety generally increased activity, particularly against mustard beetles, as in previous instances. Surprisingly, the effect on insecticidal activity of introducing an α-CN group ranged from positive to negative depending upon the nature of the alkoxyimino substituent, an effect not observed previously. The most effective esters were derived from α-cyano-4-fluoro-3-[(methoxyimino)methyl]benzyl alcohol, which was synthesised from 2-{4-fluoro-3-[(hydroxyimino)methyl]phenyl}-1,3-dioxolane.

Key words: pyrethroids, structure–activity relationships, alkoximes, insecticidal.

1 INTRODUCTION

Detailed studies of the requirements for insecticidal activity in pyrethroids[1,2] have established that variations are possible in all the regions of the molecule, provided that the appropriate overall shape and the spacing between the essential functional groups are maintained. This is illustrated (Fig. 1) by the structures of pyrethrin, deltamethrin and etofenprox.

In variations of the benzylic pyrethroids (Fig. 2), other side chains have been shown to be effective as long as they contain unsaturation. The side chain is best situated at C-3[3] when an α-cyano group enhances activity. Further to the many side chains reported earlier[2] we recently showed the effectiveness of alkoxyimino (−CH=NOR), where the unsaturation involves a hetero atom in an acyclic group.[4] In a limited number

* Part XXXVII: *Pestic. Sci.*, **28** (1990) 25–34.
‡ To whom correspondence should be addressed.

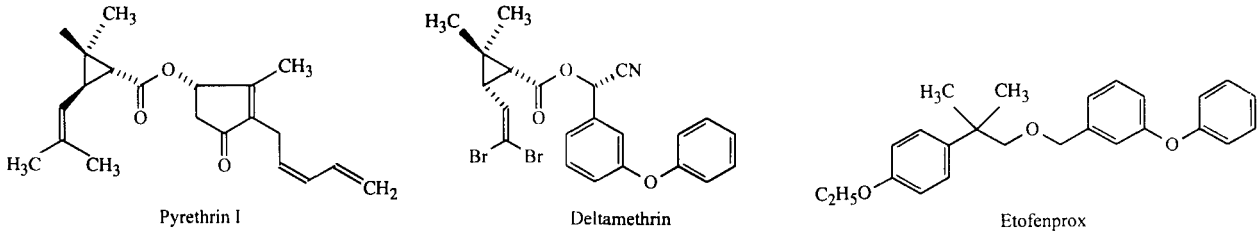


Fig. 1. Structures of established pyrethroids.

Pestic. Sci. 0031-613X/95/$09.00

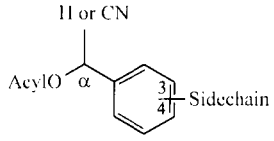


Fig. 2. General structure of benzylic pyrethroidal esters.

of cases examined, an α-cyano substituent increased activity.

Elsewhere[2] it has been shown that introduction of fluorine at position 4 of the benzylic moiety generally leads to an increase in activity. In the present study, the generality of these effects is examined in more detail to optimise activity. Thus, variations in the pyrethroidal acid, the presence or absence of an α-CN group, and of a 4-F substituent are examined in esters with various alkoxyiminomethyl side chains at position 3.

2 MATERIALS AND METHODS

2.1 General

[^{1}H] and [^{13}C]NMR spectra of synthesised compounds were determined on a JEOL GX-400 spectrometer (^{1}H frequency: 400 MHz, ^{13}C frequency: 100 MHz), using 32 and 64K data points, respectively. In all cases, samples were dissolved in deuterochloroform and tetramethylsilane was used as internal standard. In important cases, e.g. compounds in Table 1, assignments were confirmed by a 2D C-H shift correlation experiment.

Biological and some physical properties are reported in this section, but further physical properties (n_D/m.p. full NMR assignments) are given for all new esters in the Appendix (Table A1).

The term 'processed' in descriptions of syntheses implies extraction with diethyl ether (× 3) (unless otherwise specified), washing the organic layer with water (× 2), drying over anhydrous sodium sulfate and removing solvent using a rotary evaporator, to yield a residue of product.

'Petrol' refers to light petroleum distillate, b.p. 60–80°C.

2.2 Synthesis

2.2.1 2-(3-Bromo-4-fluorophenyl)-1,3-dioxolane (see Fig. 3 step (i))

A solution of trimethylsilyl trifluoromethanesulfonate (0·08 g) in dichloromethane (15 ml) was cooled to −78°C and 1,2-bis(trimethylsilyloxy)ethane (7·4 g) and 3-bromo-4-fluorobenzaldehyde (7·3 g) added. After stirring for 1 h, dry pyridine (0·8 ml) was added, the mixture poured onto saturated sodium hydrogen carbonate solution and processed. The residue was distilled to give the product (6·2 g, 70%) b.p. 90–91°C/0·6 mm Hg, [^{1}H] NMR peaks at 4·05 (m, 4H, 2 × CH_2), 5·74 (s, 1H, CHO_2), 7·11 (t, 1H, 8·5 Hz, H-5), 7.38 (ddd, 1H, 2, 4, 8 Hz, H-6), 8·27 ppm (dd, 1H, 2, 7 Hz, H-2).

2.2.2 2-(3-Formyl-4-fluorophenyl)-1,3-dioxolane (step (ii))

tert-Butyllithium (2·5 M, 10 ml) in hexane was added dropwise to a stirred solution of 2-(3-bromo-4-fluorophenyl)-1,3-dioxolane (6·3 g) in diethyl ether (500 ml) at −78°C. After 10 min, a solution of 1-formylpiperidine (4·3 g) in diethyl ether (50 ml) was added dropwise and the mixture stirred at −78°C for 30 min, followed by warming to room temperature over 1 h. The solution was poured onto saturated ammonium chloride solution and processed. The residue was eluted from a column of silica with diethyl ether + petrol (1 + 2 by volume) to give the product (2·5 g, 50%), n_D 1·5320, [^{1}H] NMR peaks at 4·07 (m, 4H, 2 × CH_2), 5·80 (s, 1H, CHO_2), 7·1 (dd, 1H, 8·5, 10 Hz, H-5), 7·73 (ddd, 1H, 2·5, 5, 8·5 Hz, H-6), 7·98 ppm (dd, 1H, 2, 6 Hz, H-2).

2.2.3 2-{4-Fluoro-3-[(hydroxyimino)methyl]phenyl}-1,3-dioxolane (step (iii))

A solution of hydroxylamine hydrochloride (1·4 g), and sodium hydroxide (0·84 g) in water (3·3 ml) and ethanol (10 ml) was stirred at room temperature. 2-(3-Formyl-4-fluorophenyl)-1,3-dioxolane (0·73 g) was added and the mixture refluxed for 4 h. On cooling, water was added and the solution processed to give the product (0·76 g, 97%), m.p. 70–72°C, [^{1}H] NMR peaks at 4.11 (m, 4H, 2 × CH_2), 6·09 (s, 1H, CHO_2), 7·09 (dd, 1H, 8·5, 9·5 Hz, H-5), 7·58 (ddd, 1H, 2·5, 5·5, 9·5 Hz, H-6), 7·74 (dd, 1H, 2·5, 6·5 Hz, H-2), 8·11 ppm (s, 1H, N=CH).

2.2.4 2-{4-Fluoro-3-[(methoxyimino)methyl]phenyl}-1,3-dioxolane (step (iv))

A mixture of 2-{4-fluoro-3-[(hydroxyimino)methyl]phenyl}-1,3-dioxolane (0·1 g), sodium hydroxide (0·02 g), tetrabutylammonium bromide (0·02 g) and water (3 ml) was stirred at room temperature and methyl iodide (0·5 ml) added dropwise. The mixture was refluxed with vigorous stirring for 2 h. On cooling, water was added and the mixture processed. The crude product was filtered through a pad of silica using ether as eluent and the filtrate evaporated to give the product (0·08 g, 75%), n_D 1·5389, [^{1}H] NMR peaks at 3·88 (s, 3H, CH_3), 4·03 (m, 4H, 2 × CH_2), 5·99 (s, 1H, CHO_2), 6·99 (t, 1H, 9 Hz, H-5), 7·52 (ddd, 1H, 2, 5, 8·5 Hz, H-6), 7·65 (dd, 1H, 2, 7 Hz, H-2), 7·94 ppm (s, 1H, N=CH).

2.2.5 4-Fluoro-3-[(methoxyimino)methyl]benzaldehyde (step (v))
Aqueous hydrochloric acid (150 g litre^{-1}; 10 ml) was added to a solution of 2-{4-fluoro-3-[(methoxyimino) methyl]phenyl}-1,3-dioxolane (1·4 g) in tetrahydrofuran (20 ml) and stirred at room temperature over 2 h. Water (20 ml) was added and the mixture processed to give the product (1·1 g, 98%) m.p. 64–66°C, [^{1}H] NMR peaks at 4·03 (s, 3H, OCH_3), 7·23 (t, 1H, 9 Hz, H-5), 7·91 (ddd, 1H, 2, 5, 8·5 Hz, H-6), 8·30 (s, 1H, N=CH), 8·37 (dd, 1H, 2, 7 Hz, H-2), 9.98 ppm (s, 1H, CHO).

2.2.6 α-Cyano-4-fluoro-3-[(methoxyimino)methyl]benzyl alcohol
A solution of 4-fluoro-3-[(methoxyimino)methyl]benzaldehyde (0·4 g) in tetrahydrofuran (6 ml) was added to sodium cyanide (0·45 g) in water (1 ml) and the mixture kept below 5°C. Sulfuric acid (400 g litre^{-1}, 1·3 ml) was added dropwise with stirring and after 10 min the solution allowed to warm to room temperature over 1 h. Water (20 ml) was added to the mixture and processed with dichloromethane to give the product (0·45 g, 98%), m.p. 50–52°C, [^{1}H] NMR peaks at 4·0 (s, 3H, $NOCH_3$), 4·5 (broad s, 1H, OH), 5·5 (s, 1H, CH), 6·9–8·2 ppm (m, 4H, AR + =CH).

2.2.7 4-Fluoro-3-[(methoxyimino)methyl]benzyl alcohol
A solution of 4-fluoro-3-[(methoxyimino)methyl]benzaldehyde (0·4 g) in diethyl ether (10 ml) was added dropwise over 15 min to a stirred suspension of lithium aluminium hydride (0.05 g), in ether (10 ml). After 2 h, water (0·15 ml) and aqueous sodium hydroxide (15%; 0·05 ml) were added and the mixture stirred for a further 15 min, filtered and the solvent evaporated to give the product (0·37 g, 92%), n_D 1·4251, [^{1}H] NMR peaks at 3·19 (broad s, 1H, OH), 3·95 (s, 3H, $NOCH_3$), 4·56 (s, 2H, CH_2), 7·00 (dd, 1H, 8·5, 10 Hz, H-5), 7·27 (ddd, 1H, 2, 4, 8 Hz, H-6), 7·72 (dd, 1H, 2, 7 Hz, H-2), 8·24 ppm (s, 1H, N=CH).

2.2.8 α-Cyano-4-fluoro-3-[methoxyimino)methyl]benzyl (1R)-cis-3(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate
A solution of (1R)-*cis*-3(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acid (0·14 g), α-cyano-4-fluoro-3-[(methoxyimino)methyl]benzyl alcohol (0.1 g), 1,3-dicyclohexylcarbodiimide (0·1 g) and 4-dimethylaminopyridine (5 mg) in dichloromethane (10 ml) was stirred at room temperature for 3 h. After filtration, the filtrate was evaporated and the residue eluted from a column of silica with diethyl ether + petrol (1 + 20 by volume) to give the product (0·16 g, 70%). When a solution of the product in hexane was cooled to 0°C one of the diastereomers crystallised out. It had [^{1}H] NMR peaks at 1·22 (s, 3H, CCH_3), 1·26 (s, 3H, CCH_3), 1·93 (d, 1H, 8 Hz, $CHCO_2$), 2·09 (t, 1H, 8·5 Hz, CHC=), 4·03 (s, 1H, OCH_3), 6·40 (s, 1H, CHCN), 6·70 (d, 1H, CH=C), 7·17 (t, 1H, 9 Hz, H-5), 7·52 (ddd, 1H, 2·5, 5, 8 Hz, H-6), 8·00 (dd, 1H, 2·5, 6·5 Hz, H-2), 8·28 ppm (s, 1H, N=CH). The mother liquors contained the other diastereomer, [^{1}H] NMR peaks at 1·30 (s, 3H, CCH_3), 1·32 (s, 3H, CCH_3), 1·92 (d, 1H, 8 Hz, $CHCO_2$), 2·05 (t, 1H, 8·5 Hz, CHC=), 4·02 (s, 1H, OCH_3), 6·34 (s, 1H, CHCN), 6·68 (d, 1H, CH=C), 7·18 (t, 1H, 9 Hz, H-5), 7·52 (ddd, 1H, 2·5, 5, 8 Hz, H-6), 8·01 (dd, 1H, 2·5, 6·5 Hz, H-2), 8·28 ppm (s, 1H, N=CH).

2.2.9 2-{3-[(Allyloxyimino)methyl]phenyl}-1,3-dioxolane
A mixture of 2-{3-[hydroxyimino)methyl]phenyl}-1,3-dioxolane (0·5 g), potassium carbonate (0·82 g) and allyl bromide (1·5 g) in dry methanol (15 ml) was refluxed for 24 h. On cooling, the mixture was filtered, the filtrate evaporated and the product dissolved in carbon tetrachloride. Solid was removed by filtration and the solvent evaporated to give the product (0·61 g, 100%), n_D 1·5496, [^{1}H] NMR peaks at 4·1 (m, 4H, 2 × CH_2), 4·7 (d, 2H, CH_2), 5·3 (m, 2H, $=CH_2$), 5·8 (s, 1H, CHO_2), 6·1 (m, 1H, $CH=CH_2$), 7·2–7·8 (m, 4H, Ar), 8·1 ppm (s, 1H, N=CH).

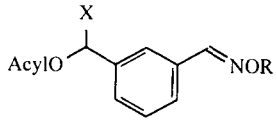
2.2.10 3-[(Allyloxyimino)methyl]benzaldehyde
2-{-[Allyloxyimino)methyl]phenyl}-1,3-dioxolane (0·61 g) was reacted as in Section 2.2.5 to give the product (0·49 g, 99%), n_D 1·5650, [^{1}H] NMR peaks at 4·7 (d, 2H, CH_3), 5·4 (m, 2H, $=CH_2$), 6·1 (m, 1H, $CH=CH_2$), 7·2–8·1 (m, 4H, Ar), 8·2 (s, 1H, N=CH), 10·0 ppm (s, 1H, CHO).

2.2.11 α-Cyano-3-[(allyloxyimino)methyl]benzyl alcohol
3-[(Allyloxyimino)methyl]benzaldehyde (0·29 g) was reacted with allyl bromide (2 g) as in Section 2.2.6 to give the product (0·25 g, 75%), n_D 1·5570, [^{1}H] NMR peaks at 4·0 (broad, 1H, OH), 4·7 (d, 2H, CH_2), 5·4 (m, 2H, $=CH_2$), 5·6 (s, 1H, CHCN), 6·1 (m, 1H, $CH=CH_2$), 7·3–7·8 (m, 4H, Ar), 8·2 ppm (s, 1H, N=CH).

2.2.12 2-{3-[(Propargyloxyimino)methyl]phenyl}-1,3-dioxolane
2-{3-[(Hydroxyimino)methyl]phenyl}-1,3-dioxolane (0·4 g) was reacted with propargyl bromide (2 g) as in Section 2.2.9 to give the product (0·49 g, 100%), n_D 1·5583, [^{1}H] NMR peaks at 2·5 (m, 1H, HC≡), 4·0 (m, 4H, 2 × CH_2), 4·8 (d, 2H, $NOCH_2$), 5·8 (s, 1H, CHO_2), 7·2–7·8 (m, 4H, Ar), 8·1 ppm (s, 1H, N=CH).

2.2.13 3-[(Propargyloxyimino)methyl]benzaldehyde
2-{3-[(Propargyloximino)methyl]phenyl}-1,3-dioxolane (0·49 g) was reacted as in Section 2.2.5 to give the product (0·39 g, 100%), n_D 1·5592, [^{1}H] NMR peaks at 2·6 (m, 1H, HC≡), 4·8 (d, 2H, $NOCH_2$), 7·3–8·2 (m, 4H, Ar), 8·3 (s, 1H,N=CH), 10·1 ppm (s, 1H, CHO).

TABLE 1
Effect of Varying the Alkoxyimino Group on Insecticidal Activity



			Relative insecticidal potency[a]			
			X = H		*X = CN*	
Entry No.	*Acyl*	*R*	*HF*[b]	*MB*[c]	*HF*[b]	*MB*[c]
1	**II**	$-CH_3$	7	3·4	18	13
2	**VI**		20	20	23	69
3	**II**	$-C_2H_5$	1·8	c 0·4	9·5	3·1
4	**VI**		7·4	7·2	7·8	19
5	**II**	$-CH_2CH{=}CH_2$	3·0	1·0	4·2	3·5
6	**VI**		22	c 8	2·9	21
7	**II**	$-CH_2C{\equiv}CH$	9·4	c 1·0	5	5·3
8	**VI**		21	16	2·9	22
9	**VI**	$-CH_2C_6H_5$	1·0	5·4	0·5	4·5

[a] Activity relative to bioresmethrin (= 100).
[b] HF = houseflies (*Musca domestica*)'
[c] MB = mustard beetles (*Phaedon cochleariae*).

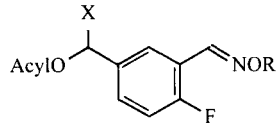
2.2.14 α-Cyano-3-[(propargyloxyimino)methyl]benzyl alcohol

3-[(Propargyloxyimino)methyl]benzaldehyde (0·2 g) was reacted as in Section 2.2.6 to give the product (0·23 g, 100%), n_D 1·5587, [^{1}H] NMR peaks at 2·5 (m, 1H, HC≡), 4·7 (d, 2H, $NOCH_2$), 5·4 (s, 1H, CHCN), 7·2–7·7 (m, 4H, Ar), 8·0 ppm (s, 1H, N=CH).

2.3 Bioassay

Insecticidal activities against *Musca domestica* L. (housefly; HF) and *Phaedon cochleariae* Fab. (mustard beetle; MB) were assessed by topical application of measured drops of solutions of the compounds in acetone as described.[5] Results (Tables 1–3) are reported

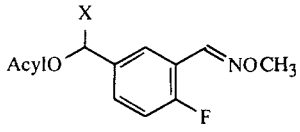
TABLE 2
Effect of Introducing a 4-F Substituent on Insecticidal Activity



			Relative insecticidal potency[a]			
			X = H		*X = CN*	
Entry No.	*Acyl*	*R*	*HF*[b]	*MB*[c]	*HF*[b]	*MB*[c]
10	**II**	$-CH_3$	11	37	7·5	72
11	**VI**		28	140	9	320
12	**II**	$-C_2H_5$	4·5	5	7·7	18
13	**VI**		20	31	7·8	72
14	**II**	$-CH_2CH{=}CH_2$	—	—	8·6	13
15	**VI**		16	42	12	79
16	**II**	$-CH_2C{\equiv}CH$	17	43	2·5	20
17	**VI**		46	130	3·2	91
18	**VI**	$-CH_2C_6H_5$	13	5·3	—	—

[a] Activity relative to bioresmethrin (= 100).
[b] Housefly (*Musca domestica*).
[c] Mustard beetle (*Phaedin cochleariae*).

TABLE 3
Effect of Varying the Acyl Group on Insecticidal Activity



		Relative insecticidal potency[a]			
		X = H		*X = CN*	
Entry No.	*Acyl*	*HF*[b]	*MB*[c]	*HF*[b]	*MB*[c]
19	**I**	2·5	19	—	—
10	**II**	11	37	7·5	72
20	**III**	21	c 50	2·3	34
21	**IV**	—	—	3·2	150
22	**V**	—	—	5·9	70
11	**VI**	28	140	9	320
23	**VII**	29	180	6	110
24	**VIII**	73	100	16	140
25	**IX**	10	12	—	—
26	**X**	—	—	NA	27
27	**XI**	—	—	6	3
28	**XII**	NA	4	—	—
29	**XIII**	NA	NA	NA	NA

[a] Activity relative to bioresmethrin (=100).
[b] House fly (*Musca domestica*).
[c] Mustard beetle (*Phaedon cochleariae*).

as relative activities, using bioresmethrin (=100) as standard.

3 RESULTS AND DISCUSSION

3.1 Synthesis

The presence of a 4-fluoro group in the alkoxyiminobenzyl moiety does not affect its chemical reactivity substantially, so many of the synthesis methods used previously[1] were equally applicable in the present series. Similarly, elucidation of the stereochemistry of the alkoxyiminomethyl side chain followed directly from the [^{1}H] and [^{13}C] NMR data (see Appendix). The key intermediate, 2-{4-fluoro-3-[(hydroxyimino)methyl]-phenyl}-1,3-dioxolane (Fig. 3), was synthesised stereospecifically as the (*E*)-isomer from commercially available 3-bromo-4-fluorobenzaldehyde, then alkylated and hydrolysed to the benzaldehydes. Subsequent reduction with lithium aluminium hydride or cyanohydrination gave the required benzyl alcohols and α-cyanobenzyl alcohols respectively, which were esterified with pyrethroidal acids. Some additional non-fluorinated α-cyanobenzyl alcohols were similarly synthesised from the previously synthesised 2-{3-[(hydroxyimino)methyl]-phenyl}-1,3-dioxolane.[4]

3.2 Bioassay results

Table 1 incorporates results from the previous[4] and present studies so that the effect of increasing sidechain length can be examined more fully while the acyl component is limited to two variations (**II** and **VI**—see Fig. 4). From the four separate sets of data (X = H or CN, species = HF or MB) activity is seen to fall as the size of R is increased. Thus, methoxyiminomethyl (entries **1** and **2**) is identified as the most effective side chain. Further, by comparing the X = H and X = CN data, increase in activity on introducing the CN group is not apparent for the bigger side chains (entries **5–9**). In some cases, reductions in activity against HF are observed.

Table 2 contains similar data for compounds with 4-H replaced by a fluorine atom. Activities against MB, in particular, are higher than those in Table 1; this species-selective increase in activity with the introduction of a 4-F substituent has been observed in pre-

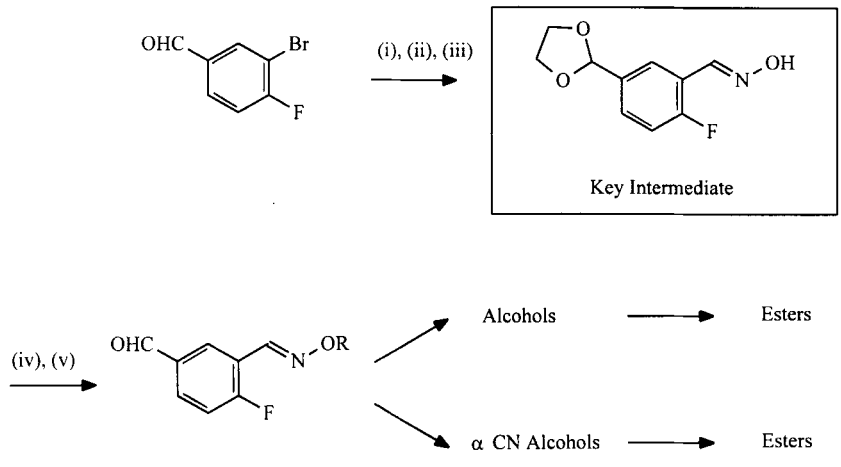


Fig. 3. Synthesis of the key intermediates and final esters. Reagents: (i) $CF_3SO_3Si(CH_3)_3$, $[(CH_3)_3SiOCH_2]_2$; (ii) *tert*-BuLi, 1-formylpiperidine; (iii) NH_2OH; (iv) Alk. RHal; (v) H^+.

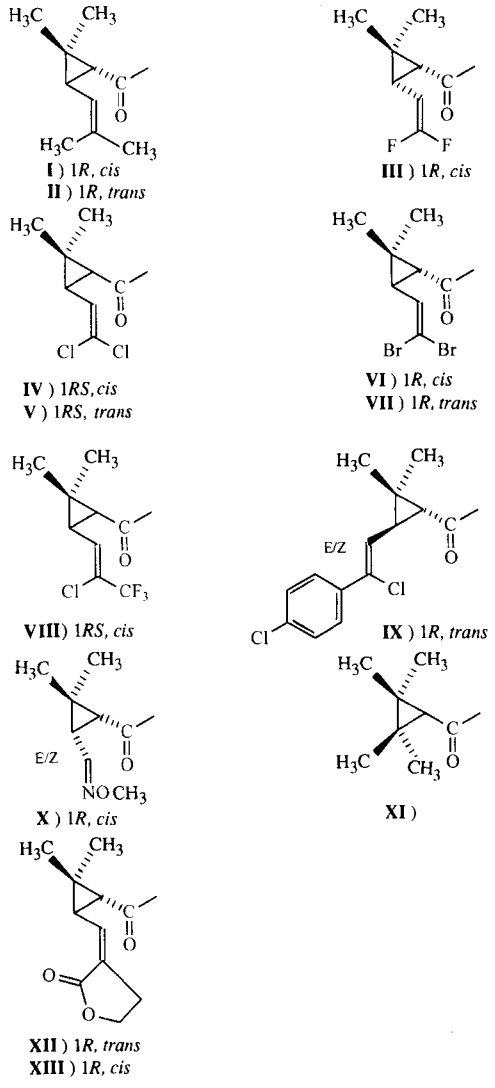


Fig. 4. Structures of the acyl groups referred to in Tables 1–3.

vious studies.[6] The trends with respect to size of side chain and introduction of an α-CN substituent are similar to those in Table 1, now reduced activity against HF is observed in all cases except when $R = C_2H_5$ (entry **12**). This negative effect of α-CN introduction has, in the past,[3] been persistent within types of structure (e.g. 4-substituted benzyl, 3-phenylbenzyl and furyl esters) so variation within a series, as observed here, is a novel effect.

Table 3 extends the study to other acyl groups (see Fig. 4). Activity is seen to rely heavily on the structure of the acid component, and the most effective variations (**VI, VII, VIII**) are those previously identified[2] as most effective with other alcohols.

In conclusion, the structural changes examined have effects that are, to a first approximation, independent of the other changes, so optimisation of the structure for insecticidal activity points clearly to (1) an acid component of known high effectiveness, e.g. **VI** (see Fig. 4), that present in deltamethrin, (2) a 4-F substituent, (3) a short substituent in the R group, and (4) depending on species, an α-H or an α-CN group.

ACKNOWLEDGEMENTS

The authors thank the British Technology Group Ltd for financial support, and Mark Hedges and Joanne Orgill for their technical support. Guidance and constant advice from Michael Elliott and Norman Janes are gratefully acknowledged.

REFERENCES

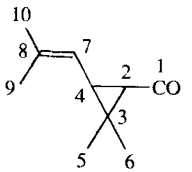
1. Elliott, M. & Janes, N. F., Synthetic pyrethroids—A new class of insecticide. *Chem. Soc. Rev.*, **7** (1978) 473–505.
2. Naumann, K. In *The Chemistry of Plant Protection*, Vol. 4, eds. W. S. Bowers, W. Ebing, D. Martin & R. Wegler. Springer-Verlag, Berlin, 1990.
3. Elliott, M., Janes, N. F., Khambay, B. P. S. & Pulman, D. A., Insecticidal activity of the pyrethrins and related compounds. Part XIII: Comparison of the effects of α-substituent in different esters. *Pestic. Sci.*, **14** (1983) 182–90.
4. Elliott, M., Farnham, A. W., Janes, N. F. & Khambay, B. P. S., The pyrethrins and related compounds. Part XXXI: Alkoxyimino-substituted esters. *Pestic. Sci.*, **22** (1988) 231–49.
5. Elliott, M., Farnham, A. W., Janes, N. F., Johnson, D. M. & Pulman, D. A., Synthesis and insecticidal activity of lipophilic amides. Part I: Introductory survey, and discovery of an active synthetic compound. *Pestic. Sci.*, **18** (1987) 191–201.
6. Baydar, A. E., Elliott, M., Farnham, A. W., Janes, N. F. & Khambay, B. P. S., The pyrethrins and related compounds. Part XXXIV. Optimisation of insecticidal activity in non-esters. *Pestic. Sci.*, **23** (1988) 247–57.

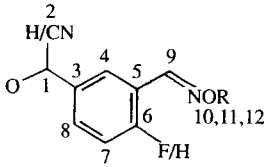
APPENDIX 1: OPTIMISATION OF INSECTICIDAL ACTIVITY IN 3-[(ALKOXYIMINO)METHYL]-4-FLUOROBENZYL ESTERS

[^{13}C] NMR data were acquired as described in Section 2.1 of the main paper. Structures are designated in the 'Cpd' column of Table A1 by a number corresponding to the entry number in Tables 1–3 of the main paper, and the absence or presence of an asterisk to indicate an α-H or an α-CN compound.

TABLE A1

[^{13}C] NMR Shifts and n_D/m.p. for Esters Synthesised





	Acid component										*Alcohol component*												
Cpd	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	n_D/m.p.
5*	170·6	34·3	30·5	20·4	22·0	33·9	120·0	136·5	25·6	18·6	62·3	116·2	132·7	129·6[a]	130·8	128·9[a]	128·8[a]	126·1[a]	147·6	75·4	133·8	118·2	1·5371
		34·1	30·3				120·3	136·4		18·5	62·4	116·3	132·8		130·7			125·9			133·4		
6*	168·5	31·0	28·8	14·9	28·1	36·4	132·4	90·9	—	—	62·2	116·1	132·3	129·6[a]	130·8	128·9[a]	128·8[a]	126·0[a]	147·5	75·4	133·8	118·2	1·5676
			29·0				132·3	90·6			62·3	116·3	132·6				128·8	126·1			133·5		
7*	170·6	34·3	30·5	20·4	22·0	33·8	120·2	136·5	25·6	18·5	62·2	116·1	132·9	129·6[a]	132·9	129·1[a]	129·0[a]	126·2[a]	148·8	62·0	79·2	74·9	1·5376
		34·1	30·3				120·3	136·4			62·3	116·3			132·8	129·3		126·4					
8*	168·5	31·0	28·4	14·9	28·1	36·5	132·2	90·9	—	—	62·4	115·9	132·3	129·7[a]	133·0	129·2[a]	129·2[a]	126·3[a]	148·7	62·0	79·3	75·0	1·5662
		31·1	29·0				132·4	90·7					132·7				126·7[a]						
9	170·2	31·8	28·3	15·0	27·6	35·7	133·4	89·4	—	—	65·8	—	132·6	129·5[a]	136·5	128·9[a]	127·0[a]	126·6[a]	148·6	76·7	137·4	—	1·5668
																					128·4		
																					128·3		
																					128·1		
9*	168·5	31·1	28·1	14·9	28·8	36·4	132·2	90·7	—	—	62·4	115·9	132·6	129·6[a]	132·6	129·0[a]	128·9[a]	126·1[a]	147·7	76·7	137·2	—	1·5644
					29·0	36·5	132·4	90·8				116·0	133·4								128·5		
																					128·4		
																					128·1		
10	172·3	34·6	29·0	20·4	22·2	33·0	121·0	135·6	18·5	25·6	65·1	—	132·7	131·2	120·1	160·4	116·0	126·5	141·9	62·3	—	—	1·5252
													(4)	(9)	(12)	(253)	(21)	(3)	(4)				
10*	170·5	34·2	30·4	20·4	22·0	33·9	120·2	136·5	18·5	25·5	61·8	116·1	128·7	130·5	121·2	161·3	116·9	126·4	140·9	62·5	—	—	1·5212
		34·4	30·6				120·3	136·6	18·6	25·6	61·9	116·2	128·8	130·6				126·6					
													(4)	(9)	(12)	(255)	(23)	(4)	(4)				
11	170·1	31·8	27·7	15·0	28·3	35·7	133·3	89·5	—	—	65·3	—	132·3	131·2	120·2	160·4	116·1	126·6	141·8	62·3	—	—	15672
													(4)	(9)	(11)	(253)	(22)	(3)	(4)				
11*	169·2	33·6	30·3	20·0	22·5	37·0	134·4	92·2	—	—	62·2	115·9	128·4	130·5	121·2	161·4	117·0	126·4	140·9	62·5	—	—	1·5563
		33·5	30·5	19·9			134·5	92·0			62·1	115·7	128·2	130·6	(12)	(256)	(22)	126·6	(4)				
													(4)	(9)				(4)					
12	172·3	34·6	29·0	20·4	22·2	33·0	121·0	135·6	25·6	18·5	65·2	—	132·6	131·1	120·3	160·4	116·0	126·5	141·6	70·1	14·7	—	1·5190
													(4)	(8)	(11)	(252)	(22)	(4)	(4)				
12*	171·7	34·4	30·6	20·4	22·0	33·9	120·2	136·4	25·6	18·5	61·8	116·1	128·6	130·5	121·4	161·4	116·9	126·5	140·7	70·4	14·6	—	1·5184
		34·2	30·4				120·3	136·6		18·6	61·9	116·2	128·7	130·3	(12)	161·3	(22)	126·3	(4)				
													(3)	(9)		(256)		(4)					
13	170·2	31·8	27·7	28·3	15·0	35·7	133·3	89·5	—	—	65·4	—	132·2	131·1	120·4	160·4	116·1	126·6	141·5	70·1	14·6	—	1·5573
													(3)	(9)	(11)	(253)	(22)	(3)	(4)				
13*	168·4	31·0	28·9	14·9	28·1	36·5	132·2	90·7	—	—	62·0	115·8	128·4	130·4	121·5	161·3	117·0	126·4	140·6	70·4	14·6	—	1·5515
	168·5		29·0				132·3	90·9			61·9	115·9	(4)	130·5	(12)	(256)	(23)	126·5	(4)				
														(9)				(4)					
14	170·5	34·4	30·6	20·4	22·0	33·8	120·2	136·5	25·6	18·6	61·8	116·1	128·6	130·5	121·2	161·3	116·9	126·4	141·3	75·7	133·6	118·4	1·5260
		34·2	30·4					136·6				116·2	128·7	130·6	(12)	(256)	(23)	126·6	(4)				
													(4)	(9)				(4)					
15	170·2	31·8	27·7	15·0	28·3	35·7	133·4	89·5	—	—	65·3	—	132·2	131·3	120·2	160·5	116·1	126·6	142·1	75·5	133·8	118·1	1·5431
													(4)	(9)	(12)	(253)	(22)	(3)	(4)				
15*	168·4	31·0	28·9	14·9	28·1	36·5	132·2	90·7	—	—	61·9	115·8	128·2	130·6	121·3	161·4	117·0	126·5	141·2	75·7	133·6	118·3	1·5571
			29·0				132·4	90·0				115·9	128·5	130·7	(12)	(256)	(22)	126·6	(4)				
													(4)	(9)				(4)					

TABLE A1

	Acid component										*Alcohol component*												
Cpd	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	n_D/m.p.
16	168·4	34·6	29·0	20·4	22·1	33·0	120·9	135·6	25·6	18·5	62·3	—	132·7 (4)	131·6 (9)	119·6 (11)	160·5 (253)	116·0 (21)	126·7 (3)	143·4 (4)	61·8 61·9	79·1	75·1 75·2	1·5282
16*	170·5	34·2 34·4	30·4 30·6	20·4	22·0	33·8	120·2	136·4 136·6	18·5 18·6	25·6	62·2	116·0 116·2	128·7 128·8 (4)	131·0 131·1 (9)	120·6 (11)	161·5 (256)	117·0 (22)	126·8 126·5 (4)	142·5 (4)	61·7 61·8	79·1	75·1	1·5286
17	170·2	31·8	28·3	15·0	27·8	35·7	133·3	89·5	—	—	65·3	—	132·3 (4)	131·7 (9)	119·7 (11)	160·6 (253)	116·2 (22)	126·8 (3)	143·4 (4)	62·0	79·3	74·9	1·5562
17*	168·4	31·0	28·1 28·2	14·9	28·9 29·0	36·5	132·2 132·3	90·8 91·0	—	—	62·3	115·7 115·9	128·2 128·5 (4)	130·1 (9)	120·7 (12)	161·6 (256)	117·1 (23)	126·7 126·8 (4)	142·5 (4)	61·8 61·9	79·1	75·1 75·2	1·5557
18	170·2	31·8	27·7	15·0	28·3	35·7	133·3	89·5	—	—	65·3	—	132·2 (4)	131·3 (9)	120·2 (11)	160·5 (253)	116·1 (22)	126·7 (3)	142·3 (5)	76·7	137·2 128·4 128·3 128·1	—	1·5690
19	170·8	31·1	26·7	14·8	28·8	32·5	118·0	134·9	18·3	25·9	64·7	—	132·8 (3)	131·2 (9)	120·0 (11)	160·3 (252)	116·0 (22)	126·5 (3)	141·8 (4)	62·2	—	—	1·5249
20	170·6	29·9	26·3	14·6	28·3 (7)	26·7 (16, 28)	73·8 (285, 289)	157·1	—	—	65·1	—	132·4 (4)	131·2 (9)	120·2 (12)	160·5 (253)	116·1 (22)	126·6 (3)	141·8 (4)	62·3	—	—	1·5042
20*	168·7	29·4	27·6	14·5	28·1	27·7 27·8 (7)	73·1 73·2 (17, 28)	~157	—	—	61·7	115·9 116·0	128·6 128·4 (4)	130·6 (9)	121·2 (12)	161·3 (256)	117·0 (22)	126·5 (4)	140·9 (4)	62·5	—	—	1·5083
21*	168·5	31·0	28·9 29·1	14·8	28·1	33·5	123·7 123·8	122·1 121·9	—	—	61·9	115·8 115·9	128·2 128·5 (4)	130·6 (9)	121·2 (12)	161·3 (256)	117·0 (22)	126·5 126·4 (4)	140·9 (5)	62·5	—	—	1·5410
22*	169·3 169·2	33·8	30·4 30·5	20·0	22·4	33·9	125·9 126·0	~122	—	—	62·1 62·2	115·9 115·7	~129	130·5 130·6 (9)	~121	~161	117·0 (22)	126·4 126·6 (4)	140·9 (4)	62·5	—	—	1·5440
23	170·8	36·1	29·2	20·0	22·7	34·4	135·4	90·9	—	—	66·5	—	132·3 (4)	131·3 (9)	120·2 (11)	160·4 (253)	116·1 (22)	126·5 (4)	141·8 (4)	62·3	—	—	94–96°C
23*	168·5	31·0	29·1	14·9	28·2	36·5	132·3	90·7	—	—	61·9	115·9 116·3	128·2 (4)	130·6 (9)	121·2 (12)	161·4 (256)	117·0 (22)	126·6 (4)	140·9 (4)	62·5	—	—	1·5620
24	170·0	32·8[a]	28·9	14·9	28·3	31·0 (5)	129·9 (38)	121·8 (271)	120·4	—	65·5	—	132·1 (4)	131·3 (8)	120·2 (12)	160·5 (252)	116·2 (21)	126·7 (4)	141·8 (4)	62·3	—	—	1·4990
24*	168.3 168·4	32·0[a]	30·1 29·9	14·8	28·2 28·1	31·7	128·7 (5)	122·7 (38)	120·3 (271)	—	62·2 62·1	115·8 115·7	128·0 128·4	130·7 130·6 (9)	121·3 (12)	161·4 (256)	117·1 (22)	126·6 126·5 (4)	140·8 140·9 (4)	62·5	—	—	1·5069
25	171·2 170·9	33·9 33·6	29·7 29·8	20·3 20·0	22·7 22·3	35·3 35·2	125·1 127·1	—	—	—	65·5	—	132·3 132·4 (4)	131·3 131·4 (9)	120·1 (11)	160·4 (253)	116·2 (22)	126·6 126·7 (4)	141·8 (4)	62·3	—	—	1·5550
26	168·6	32·4	28·8 28·6	14·6 14·7	27·9 28·0	31·3 31·4	147·0 145·2	—	—	—	61·8 62·0	115·9 115·8	128·2 128·5 (4)	130·7 130·6 (9)	121·2 (12)	161·3 161·2 (256)	117·0 (22)	126·5 126·6 (4)	140·8 140·9 (4)	62·5	—	—	1·5201
27*	169·8	35·0	32·1 32·3	16·5	23·4	—	—	—	—	—	61·3	116·4	128·9 (4)	130·6 (9)	121·1 (12)	161·3 (255)	116·9 (22)	126·4 (4)	141·0 (4)	62·5	—	—	1·5182
28	169·7	33·4[a]	29·5	15·0	28·6	34·0[a]	135·9	126·4	25·3	170·7	65·3	—	132·3 (4)	131·5 (9)	120·0 (11)	160·4 (253)	116·1 (22)	126·6 (4)	141·7 (4)	62·3	—	—	82–84°C
29	170·8	34·1	31·0	20·4	22·4	36·3	137·7	126·7	25·3	170·6	65·4 65·7	—	132·1 (4)	131·3 (8)	120·2 (11)	160·4 (253)	116·1 (22)	126·6 (4)	141·7 (4)	62·3	—	—	s.s.
29*	170·7 170·6	35·1 34·8	32·2 32·0	20·4 20·3	22·3 22·2	35·4 35·2	136·6 136·4	127·6 127·4	25·4 25·3	169·2 169·1	65·4 65·5	115·8 115·7	128·0 128·1 (4)	130·7 130·6 (9)	121·2 (12)	161·4 (254)	117·1 (22)	126·4 126·6 (4)	140·8 (4)	62·4 62·3	—	—	s.s.

[a] 50/50 mixture of *E*/*Z* isomers. * α-CN esters.