Pestic. Sci. 1995, **44**, 269–275

The Pyrethrins and Related Compounds Part XXXIX*— Structure–Activity Relationships of Pyrethroidal Esters with Cyclic Side Chains in the Alcohol Component against Resistant Strains of Housefly (*Musca domestica*)

Andrew W. Farnham & Bhupinder P. S. Khambay‡

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

(Received 10 February 1994; revised version received 17 October 1994; accepted 28 February 1995)

Abstract: Activities of a range of pyrethroidal esters, incorporating structural variations in all regions of the acid and alcohol components, have been measured against two fully characterised and homozygous resistant strains of *Musca domestica* L. (*kdr* and *super-kdr*). The results, limited in this paper to esters of alcohols with *cyclic* side chains, indicate uniform resistance to the *kdr* strain across the whole range of structural variations. Against the *super-kdr* strain, while variation in the acid component has little effect, the resistance factor is sensitive to the nature of the alcohol component, in particular on whether it contains an α-cyano substituent.

Key words: pyrethroids, resistance, *kdr*, *super-kdr*, structure–activity relationships, *Musca domestica*.

1 INTRODUCTION

Resistance of insects has developed to a stage where the commercial and environmental consequences are substantial.[1] Since the more photostable synthetic pyrethroids, suitable for use in agriculture, were introduced in the 1970s,[2] instances of resistance in the field have become increasingly frequent.[1] Analysis of some of these cases has defined the major mechanisms of resistance as either metabolic or involving modifications at the site of action. The latter, the most important resistance mechanisms for pyrethroids and DDT in houseflies,[3–5] are known as the knock-down resistance factors *kdr* and its allele *super-kdr*. These have been fully characterised in substrains of housefly homogeneous specifically for each factor.[6] Both provide cross-resistance between all pyrethroids and DDT-type insecticides. *kdr*-like resistance has also been implicated to account for resistance to pyrethroids in other insects including members of the Lepidoptera, Diptera, Homoptera, cockroaches and ticks,[7–13] highlighting the wide-ranging importance of this type of resistance mechanism. It has been studied extensively using electrophysiological techniques,[14–17] but its response to changes in the structure of the insecticide has received less attention. In our previous study,[6] relationships (SARs) between chemical structure of pyrethroids and levels of resistance in housefly strains homozygous for knockdown resistance were found: bioassays with nine pyrethroids demonstrated that flies

* Part XXXVIII. *Pestic Sci.*, **44** (1995) 261–8.
‡ To whom correspondence should be addressed.

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

TABLE 1
Bioassay Results against Susceptible, kdr and super kdr Strains of Houseflies (*Musca domestica* L.)

	Compound[a]	*Susceptible strain* LD_{50} (*μg per fly*)	*kdr strain* *RF (I)*	*Super-kdr strain* *RF (II)*
A1	Bioresmethrin	0·0034	16	53
B1	Cismethrin	0·032	13	59
C1	NRDC 173	0·0020	14	75
D1		0·0056	11	48
E1		0·0089	12	53
G1		0·0047	12	62
I1	RU15525	0·056	23	100
J1	NRDC 108	0·0046	15	63
A2		0·012	16	68
D2	NRDC 147[a]	0·0071	12	42
E2	NRDC 167[a]	0·0043	8·6	56
G2	NRDC 157	0·0034	18	91
H2		0·0022	13	68
J2		0·027	24	93
K2		0·030	9·7	60
A3		0·0065	11	130
B3		0·015	16	150
E3	alpha-cypermethrin[b]	0·0011	28	250
G3	deltamethrin[c]	0·00027	31	560
H3	lambda-cyhalothrin[b]	0·00075	13	290
K3	s-fenvalerate[d]	0·0049	20	170
L3	flucythrinate	0·0082	12	120
E4[e]		0·0017	14	200
G4		0·0012	16	370
K4		0·012	34	120
E5		0·014	23	71
F5		0·0088	18	72
G5		0·0086	13	63
H5	bifenthrin	0·010	13	69
G6		0·017	18	88
G7		0·0073	15	95
G8		0·0025	24	520
G9		0·093	10·3	28
E10		0·014	9·3	500
A11	NRDC 121	0·11	15	45
F12		0·079	27	>200
F13		1·8	6·7	>200

[a] See Fig. 2 for structure.
[b] (*αS,1Rcis* + *αR,1S,cis*)isomers.
[c] *α-S* isomer.
[d] *S,S*-isomer.
[e] 1*R*-isomer.

with *kdr* exhibited weak to moderate resistance to them whilst those with *super-kdr* demonstrated a definite gradation in resistance that could be related to the nature of the alcoholic moiety. In addition, Pedersen[18] tested non-ester pyrethroids (e.g. etofenprox) without firmly identifying any SARs, and recently Takada *et al.*[19] confirmed our previous findings, using a different strain of resistant flies. Here we report a detailed extension of our previous study with a much wider range of related compounds chosen specifically to explore effects of

structural change on activity against *kdr* and *super-kdr* strains of housefly, and using particular isomeric forms of the compounds instead of commercial mixtures.

2 EXPERIMENTAL

2.1 Chemicals

Six of the compounds tested were gifts from commercial companies: RU15,525 from Roussel-Uclaf; alpha-cypermethrin from Shell; lambda-cyhalothrin from Zeneca; flucythrinate from American Cyanamid; *S*-fenvalerate from Sumitomo and bifenthrin from FMC. The remainder were available from previous work[20–26] or synthesised by esterification, using one of the two previously described procedures[27] to combine the acid and alcohol components. Most of the acids used (**C, D, E,F, G, J**) were available from previous work,[20–23] while others (**A, B**) were gifts from Roussel-Uclaf. Acid **K** was made by the published method.[28] Similarly, the alcohols were available either commercially (**2**) or from previous work (**1**,[29] **3**,[24] **12**, **13**[30]) or were a gift from Bayer (**4**). Acid **H** and alcohol **5** were obtained from bifenthrin by hydrolysis.

Physical properties for the synthesised esters, and the intermediates obtained by hydrolysis, including [^{1}H] and [^{13}C] NMR spectra (determined for deutero-chloroform solutions on a JEOL GX 400 spectrometer at 400 and 100 MHz respectively) are given in the Appendix.

2.2 Insect strains used

The susceptible strain of houseflies (*Musca domestica* L.) used in this work is designated Cooper S and is the one that has been used throughout the studies on structure–activity relationships in pyrethroids. Isolation of the resistant strains of this species, kdr_{Latina} and $super\text{-}kdr_{3D}$, has been described fully.[6] They have been maintained with continual checks for homozygosity and retention of vigour, using the described techniques.[31]

2.3 Bioassay

The bioassay procedure for establishing LD_{50} values from mortality data for flies treated topically with various concentrations of test solutions as 1-μl droplets in acetone has been described previously.[31] Each LD_{50} value is a result calculated from at least two tests.

The results for the 37 compounds examined against the three strains of houseflies are presented in Table 1. LD_{50} values are in μg per fly. Each resistance factor (RF) is obtained by dividing the LD_{50} value for the resistant strain by the LD_{50} value for the susceptible strain. These values therefore represent relative responses to modifications, independent of intrinsic toxicity.

2.4 Statistical analysis

As discussed by Snedecor & Cochran,[32] the appropriate method of analysis for skewed data, in which deviation is proportional to the mean rather than independent of it, involves a logarithmic transformation. This type of variation would be expected for the resistance factors in Table 1, since they could vary from zero to infinity and effects on them are likely to be proportional rather than additive. Consequently, logarithms of the group of resistance factors under consideration were analysed to find the mean value and standard deviation for the group. Anti-logs of these two values gave the numbers in the text, separated by an $x/\div$ symbol (rather than a $+/-$) because of the antilogging step.

3 DISCUSSION

The 37 pyrethroidal esters tested are derived from 13 representative pyrethroidal acids and 11 pyrethroidal alcohols with *cyclic* side chains (alcohols with *acyclic* side chains are considered in a subsequent paper[33]) (see Fig. 1). Results from the *kdr* strain showed a remarkably consistent level of resistance, as represented by RF (I) in Table 1. A statistical analysis applied to the whole set gave a mean value of 15·3 with the very low standard deviation of $x/\div$ 1·45. Attempts to correlate small variations within this range with structural variation in either the acid or alcohol component were accordingly unsuccessful. The consistent level of resistance observed also indicates a lack of dependence of resistance factor on the intrinsic activity of the insecticide to susceptible insects. This last conclusion is also applicable to the *super-kdr* factors.

In contrast to the lack of dependence of RF (I) on structure, results from the *super-kdr* strain showed RFs (II) that were not only much higher (mean 100·3) but also spread over a significantly wider range ($x/\div$ 2·14). Closer examination showed that the various RF values have clusters when considered in terms of the alcoholic components. The highest numbers in the RF (II) column arise from esters with α-cyano groups in the alcohol (Fig. 2, compounds **3**, **4**, **8**, **10**,**13**). When analysed as a single set, they give a mean RF of 240 ($x/\div$ 1·80). These results appear to be valid for a range of compounds of widely differing structures and with widely differing intrinsic toxicities. The remaining esters, derived from alcohols (Fig. 2, compounds **1**, **2**, **5**, **6**, **7**, **9**, **11**, **12**) without an α-cyano on the alcoholic carbon,

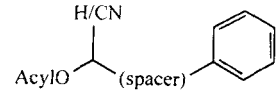


Fig. 1. General structure for pyrethroid esters examined.

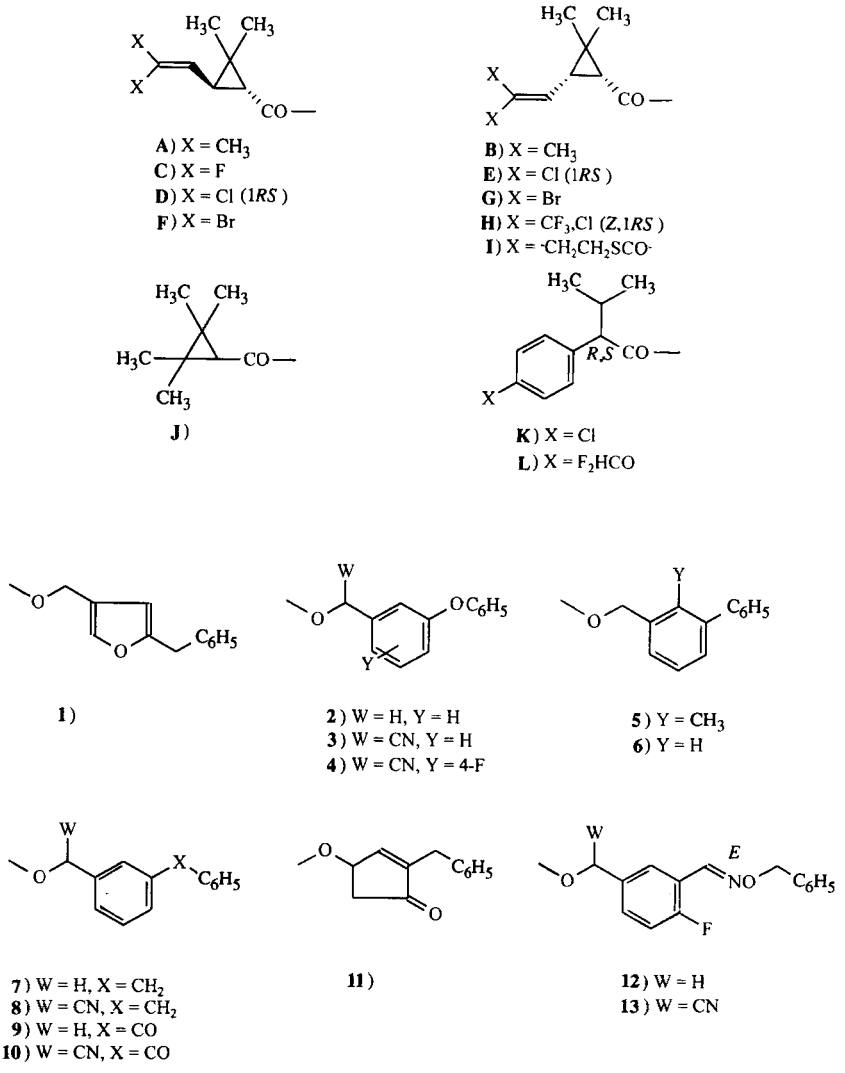


Fig. 2. Structures of alcoholic and acidic components referred to in Table 1.

considered as a set, have lower mean RF (II) of 63·6 ($x/\div$ 1·35). The small standard deviation in these two analyses indicates a clear dependence of resistance to the *super-kdr* strain on the structure of the alcoholic component.

A large structural contrast in the types of spacer group present, namely 3-furylmethyl (alcohol **1**), cyclopentenonyl (alcohol **11**) and benzyl (**2–10**, **12**, **13**), appears not to have a significant influence on RF values. Similarly an attempt to cluster the results based on the structure of the acidic component gave mean values with larger standard deviations, e.g. for acid **G** the value was 127 ($x/\div$ 2·88), so like the spacer group, features in the acid component such as stereochemistry across the ring, and substituents on the side chain, appear to have smaller influence on RF (II).

In conclusion, these results indicate that *kdr* applies equally to all pyrethroids examined in the paper suggesting that the modification involved may not be at the primary site where the insecticide binds, but in the region responsible for relaying the perturbation whereby the ion conductance properties of the sodium channel are modified. However, resistance of *super-kdr* flies towards ester pyrethroids is strongly influenced by the nature of the alcohol component, as reflected by the large variation in RF (II) (Table 1), in particular by the presence or absence of an α-CN in substituted benzyl esters. Such structural dependence implies that the modification in the *super-kdr* strain is at the pyrethroid binding site.

This study therefore confirms the importance of the alcohol component, but not the acid component, in determining levels of resistance to the *super-kdr* mechanism, and indicates the need for further work concentrating on this region of the molecule.

ACKNOWLEDGEMENT

The authors thank David Beddie, Liz Cook, Mark Hedges, Simon Kingham, Andrew Peel, Sarah Perryman and Jean White for technical assistance, Norman

Janes and Michael Elliott for advice and help in preparing the manuscript, and the British Technology Group for financial support.

REFERENCES

1. Georghiou, G. P., Overview of insecticide resistance. In *Managing Resistance to Agrochemicals*, ed. M. B. Green, H. M. LeBaron & W. K. Moberg. ACS Symposium Series No. 421, American Chemical Society, Washington, 1990, pp. 18–41.
2. Elliott, M., The pyrethroids: Early discovery, recent advances and the future. *Pestic. Sci.*, **27** (1989) 337–51.
3. Keiding, J., Resistance in the housefly. In *Pesticide Management and Insecticide Resistance*, ed. D. L. Watson & A. W. A. Brown. Academic Press, New York, 1977, pp. 261–302.
4. Sawicki, R. M., Resistance to pyrethroid insecticides in arthropods. In *Progress in Pesticide Chemistry and Toxicology*, Vol. 5. *Insecticides*, ed. D. H. Hutson & T. R. Roberts. John Wiley, Chichester, 1985, pp. 143–92.
5. Soderlund, D. M. & Bloomquist, J. R., Molecular mechanisms of insecticide resistance. In *Pesticide Resistance in Arthropods*, ed. R. T. Roush & B. E. Tabashnik. Chapman and Hall, New York, 1990, pp. 58–96.
6. Farnham, A. W., Murray, A. W. A., Sawicki, R. M., Denholm, I. & White, J. C., Characterisation of the structure–activity relationships of *kdr* and two variants of *super-kdr* to pyrethroids in the housefly (*Musca domestica* L.). *Pestic. Sci.*, **19** (1987) 209–20.
7. Amichot, M., Castella, C., Cuany, A., Berge, J. B. & Pauron, D., Target modification as a molecular mechanism of pyrethroid resistance in *Drosophila melanogaster*. *Pestic. Biochem. Physiol.*, **44** (1992) 183–90.
8. Taylor, M. F. J., Heckel, D. G., Brown, T. M., Kreitman, M. E. & Black, B., Linkage of pyrethroid insecticide resistance to a sodium channel locus in the tobacco budworm. *Insect. Biochem. Molec. Biol.*, **23** (1993) 763–75.
9. Free, D. J., Archibald, Ker, K. W. & Cole, K. J., Occurrence of pyrethroid resistance in pear psylla (Homoptera: Psyllidae) populations from southern Ontario. *J. Econ. Entomol.*, **83** (1990) 2159–63.
10. Scott, J. G., Mellon, R. B., Kirino, O. & Georghiou, G. P., Insecticidal activity of substituted benzyl dichlorovinylcyclopropanecarboxylates on susceptible and *kdr*-resistant strains of the southern house mosquito, *Culex quinquefasciatus*. Nihon Noyaku Gakkaishi (*J. Pestic. Sci.*), **11** (1986) 475–7.
11. Gunning, R. V., Easton, C. S., Balfe, M. E. & Ferris, I. G., Pyrethroid resistance mechanisms in Australian *Helicoverpa armigera*. *Pestic. Sci.*, **33** (1991) 473–90.
12. Scott, J. G. & Matsumura, F., Evidence for two types of toxic actions of pyrethroids on susceptible and DDT-resistant German cockroaches. *Pestic. Biochem. Physiol.*, **19** (1983) 141–50.
13. Nicholson, R. A., Chalmers, A. E., Hart, R. J. & Wilson, R. G., Pyrethroid action and degradation in the cattle tick (*Boophilus microplus*). In *Neurotox '79: Insect neurobiology and pesticide action*. Society of Chemical Industry, London, 1980, pp. 289–95.
14. Miller, T. A., Kennedy, J. M. & Collins, C., CNS insensitivity to pyrethroids in the resistant *kdr* strain of houseflies. *Pestic. Biochem. Physiol.*, **12** (1979) 224–30.
15. Ahn, Y. J., Shono, T., Hido, O. & Fukahami, J. I., Mechanisms of resistance to pyrethroids and 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl) ethane in the house fly *Musca domestica* L. *Pestic. Biochem. Physio.*, **31** (1988) 46–53.
16. Nicholson, R. A. & Miller, T. A., Multifactorial resistance to transpermethrin in field-collected strains of the tobacco budworm *Heliothis virescens* F. *Pestic. Sci.*, **16** (1985) 561–70.
17. Peyronet, O., Pikchou, Y. & Delorme, R., Biological responses and electrophysiological effects of topical application of deltamethrin on a resistant and a susceptible strain of *Drosophila melanogaster* Meig. *Pestic. Biochem. Physiol.*, **47** (1993) 185–98.
18. Pedersen, L. E. K., The potency of cyclopropane pyrethroid ethers against resistant strains of the house fly *Musca domestica*. *Experientia*, **42** (1986) 1057–8.
19. Takada, Y., Kawada, H. & Hirano, M., The differences in contribution of *kdr* factor on the third chromosome to the resistance of some pyrethroids in houseflies. In *Proc. XIX International Congress of Entomology* (1992) Abstract no. #18.
20. Barlow, F., Elliott, M., Farnham, A. W., Hadaway, A. B., Janes, N. F., Needham, P. H. & Wickham, J. C., Essential features for insecticidal activity in chrysanthemates and related cyclopropane esters. *Pestic. Sci.*, **2** (1971) 115–18.
21. Elliott, M., Farnham, A. W., Janes, N. F., Needham, P. H. & Pulman, D. A., Insecticidal dihalovinyl analogues of *cis* and *trans* chrysanthemates. *Pestic. Sci.*, **6** (1975) 537–42.
22. Fujimoto, K., Itaya, N., Okuno, Y., Kadota, T. & Yamaguchi, T., A new insecticidal pyrethroid ester. *Agr. Biol. Chem.* **37** (1973) 2681–2.
23. Burt, P. E., Elliott, M., Farnham, A. W., Janes, N. F., Needham, P. H. & Pulman, D. A., Geometrical and optical isomers of 2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropanecarboxylic acid and insecticidal esters with 5-benzyl-3-furylmethyl and 3-phenoxybenzyl alcohols. *Pestic. Sci.*, **5** (1974) 741–9.
24. Elliott, M., Farnham, A. W., Janes, N. F., Needham, P. H. & Pulman, D. A., Synthetic insecticide with a new order of activity. *Nature* (*London*), **248** (1974) 710–11.
25. Elliott, M., Janes, N. F. & Payne, M. C., Synthesis of insecticidal esters of 4-hydroxycyclopent-2-enones (norrethrins). *J. Chem. Soc.*(*C*) (1971) 2548–51.
26. Elliott, M., Janes, N. F., Khambay, B. P. S. & Pulman, D. A., Comparison of the effects of α-substituents in different esters. *Pestic. Sci.*, **14** (1983) 182–90.
27. Elliott, M., Farnham, A. W., Janes, N. F. & Khambay, B. P. S., Effective combinations in the gem-dimethyl-central group region of non-ester pyrethroids. *Pestic. Sci.*, **22** (1988) 231–49.
28. Miyakado, M., Ohno, M., Okuno, Y., Hirano, M., Fujimoto, K. & Yoshioka, H., Optical resolution and determination of absolute configuration of α-isopropyl-4-substituted phenylacetic acids and insecticidal activities of their 5-benzyl-3-furylmethyl esters. *Agric. Biol. Chem. Tokyo*, **39** (1975) 267–72.
29. Elliott, M., Janes, N. F. & Pearson, B. C., 5-Substituted 3-furoates and 3-thenoates, intermediates for synthesis of insecticidal esters. *J. Chem. Soc.* (*C*) (1971) 2551–4.
30. Beddie, D. G., Farnham, A. W. & Khambay, B. P. S., Optimisation of insecticidal activity in 3-[(alkoxyimino) methyl]-4-fluorobenzyl esters. *Pestic. Sci.*, **44** (1995) 261–9.
31. Farnham, A. W., Genetics of resistance of pyrethroid-selected houseflies, *Musca domestica* L. *Pestic. Sci.*, **4** (1973) 513–20.
32. Snedecor, G. W. & Cochran, W. G., *Statistical Methods*. Iowa State University Press, USA 6th edn, 1967, pp. 329–30.
33. Farnham, A. W. & Khambay, B. P. S., Structure–activity relationships of pyrethroidal esters with acyclic side chains in the alcohol component against resistant strains

of houseflies (*Musca domestica* L.). *Pestic. Sci.*, **44** (1995) 277–82.
34. Plummer, E. L., Cardis, A. B., Martinez, A. J., Vansaun, W. A., Palmere, R. M., Pincus, D. S. & Stewart, R. R., Pyrethroid insecticides derived from substituted biphenyl-3-ylmethanols. *Pestic. Sci.*, **14** (1983) 560–70.
35. Bentley, P. D., Cheetham, R., Huff, R. K., Pascoe, R. & Sayle, J. D., Fluorinated analogues of chrysanthemic acid. *Pestic. Sci.*, **11** (1980) 156–64.

APPENDIX 1

Acid H and Alcohol 5

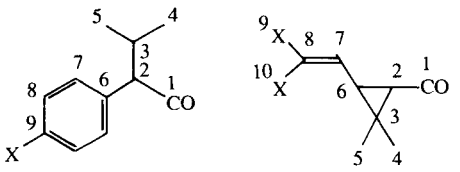
A mixture of bifenthrin (1·0 g) and potassium hydroxide (0·3 g) in methanol (20 ml) and water (4 ml) was boiled under reflux for 2 h, and concentrated under reduced pressure. The residue was shaken with water (100 ml) and ether (100 ml). The layers were separated and washed with ether (2 × 50 ml) and 2 M aqueous sodium hydroxide (2 × 50 ml) respectively.

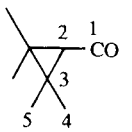
The combined ether layers were dried (anhyd. calcium chloride) and evaporated to dryness to give 2-methyl-3-phenylbenzyl alcohol (0·32 g) 34 m.p. 55–57°, [^{1}H]NMR peaks at 2·0 ppm (s, 1H, OH), 2·2 (s, 3H, CH_3), 4·7 (s, 2H, CH_2), 7·0–7·5 ppm (m, 8H, aryl Hs) and [^{13}C]NMR peaks at 15·8 ppm (CH_3), 63·8 (CH_2), 125·5, 126·6, 126·8, 129·5 (each 1C, aryl CHs), 128·0, 129·3 (each 2Cs, 4 of Ph CHs), 133·5, 139·2, 142·0, 142·7 (4 × quaternary Cs).

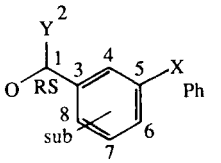
The aqueous layer was acidified, extracted with diethyl ether (3 × 50 ml), and the combined organic layers evaporated to dryness to give (1*R*,cis)-(*Z*)-2,2-dimethyl-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-cyclopropanecarboxylic acid (0·46 g), m.p. 105–107°, [^{1}H]NMR peaks at 1·32 (s, 6H, 2 × CH_3), 1·99 (d, 1H, 9 Hz, H-1), 2·25 (t, 1H, 9 Hz, H-3), 6·86 ppm (d, 1H, 9Hz, CH=) and [^{13}C]NMR peaks at 14·9, 28·5 (2 × CH_3), 29·7 (C-2), 31·7 (C-1), 32·7 (C-3), 120·4 (q, 272 Hz, CF_3), 122·4 (q, 38 Hz, C2′), 129·6 (q, 5 Hz, C1′), 177·3 ppm (CO_2H).

TABLE A1

[^{13}C] NMR Shifts for Esters Synthesised







Acid *Alcohol*

	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*Other*
2H	170·0	32·8[a]	28·8	14·9	31·0[a]	130·1 (5)	121·7 (38)	120·5 (271)	—	—	65·9	···	137·8	118·3[b]	157·6[c]	118·5[b]	130·0	122·7	156·9[c]	119·1	129·8	123·5	···
2J	171·8	35·6	30·3	23·5	16·6	—	—	—	—	···	65·0	—	138·6	118·2	157·5[a]	118·2	129·8	122·6	157·0[a]	119·0	129·7	123·4	—
2K	173·3	59·3	31·9	21·3	20·1	133·1[a]	129·8	128·6	136·6[a]	—	66·0	—	137·8	118·4	157·5[b]	118·4	129·8	122·5	156·9[b]	119·0	129·8	123·5	
3A	170·5	33·9[a]	30·4	22·0	20·4	34·3[a]	120·3	136·5	18·5	25·6	62·2	116·3	133·9	117·5	158·1[b]	120·0	130·5	122·1	156·2[b]	119·3	130·0	124·0	···
		33·8	30·2			34·0	120·2	136·3			62·1	116·2	133·8	117·7				122·0	156·3	119·4			
3B	168·9	30·6	28·1	14·7	28·6	33·5	119·9	136·3	18·5	25·6	61·7	116·3	134·1	117·7	158·1[b]	119·9	130·5	122·1	156·3[b]	119·3	130·0	124·0	
			27·9			33·6		136·0	18·4			116·4	133·9	117·6	158·0			122·0					
4E	168·4	31·0	28·1	14·8	29·1	33·5	124·0	120·9	—	—	61·8	115·9	128·5	124·0	144·7	155·5	117·9	120·8	156·4	117·8	130·0	124·0	
		30·9			28·9			120·8				115·7	(8)	(12)	(253)	(19)	(2)			117·7			
4G	168·3	30·9	29·0	14·9	28·1	36·5	132·3	90·9	···	—	61·8	115·8	128·3	124·0	144·7	155·5	117·9	120·8	156·4	117·8	130·0	123·9	--
	168·4	31·0	28·8				132·2	90·7				115·7		(7)	(12)	(253)	(19)	(2)		117·7			
4K	171·5	58·7	32·3	21·2	20·0	133·7[a]	129·7	128·9	135·2	—	62·0	115·5	128·4	123·7	144·7	~155	117·9	120·5	156·4	117·8	130·0	124·0	--
	171·4	58·5	32·1	21·1					135·0		62·2	115·3		(8)	(?)	(?)	(19)	(2)		117·7	129·9		
5E	170·4	31·8	27·6	15·0	28·4	32·6	124·8	120·7	—	—	65·2	···	134·4[a]	134·4[a]	141·8[a]	126·9[b]	125·6[b]	130·3[b]	142·9[a]	128·1	129·3	128·3	16.2 (CH_3)
5F	170·9	36·0	29·0	22·7	20·1	34·6	133·5	90·9	—	—	65·2	···	134·4[a]	134·5[a]	141·8[a]	126·9[b]	125·6[b]	130·3[b]	143·0[a]	128·1	129·3	128·4	16·2 (CH_3)
5G	170·4	31·9	27·6	15·1	28·4	35·7	133·5	89·4		—	65·5	···	134·4[a]	134·4[a]	141·9[a]	126·9[b]	125·6[b]	130·3[b]	143·0[a]	128·1	129·4	128·3	16·2 (CH_3)
6G	170·3	31·9	27·7	15·1	28·4	35·7	133·5	89·4		—	65·3	···	141·7[a] ←	(140.8[a])						127·1–129·1		→	--
11G	168·4	30·9	29·0	14·9	28·1	36·5	132·2	90·9	—	—	62·3	—	131·4	129·1[a]	136·8	131·8[a]	132·9[a]	129·3[a]	138·6	130·0	128·5	132·4	195·4 (CO)
		31·0	28·8			36·4		90·8															

[a,b,c] Peak assignments may be transposed.

Double sets of data are for mixtures of diastereomers.

Figures in parentheses represent coupling constants (in Hz) to fluorine.