

VII. STEREOISOMERS OF CYCLOPROPANECARBOXYLIC ESTERS OF THE PYRETHROID SERIES

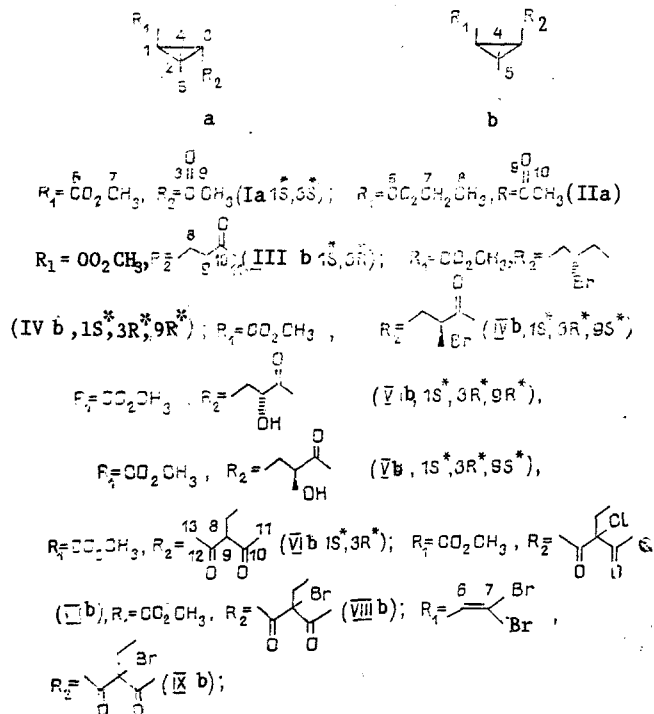
L. M. Khalilov, A. A. Fatykhov,
V. S. Sultanova, F. Z. Makaev,
F. Z. Galin, G. A. Tolstikov, and
A. A. Panasenko

UDC 543.422.25+632.951.2

The ¹³C spectra of 25 new substituted cyclopropanes of the pyrethroid series have been investigated and a stereochemical assignment has been made of the stereoisomers formed. As the criterion for stereochemical assignment it is proposed to use the values of the chemical shifts for the α-carbon atoms of the substituents in the cyclopropane ring.

Functionally substituted cyclopropanes find wide use in the synthesis of many biologically active compounds — in particular, pyrethroids, attractants, pheromones, and drugs [2]. The methods of ¹³C NMR spectroscopy are widely used for the stereochemical identification of substituted cyclopropanes.

We have studied the ¹³C NMR spectra of a series of substituted cyclopropanes used in the synthesis of pyrethroids (I)-(XXV), have investigated the dependence of the chemical shifts on the stereochemistry of the molecules, and have proposed criteria for the spectral identification of the stereoisomers.



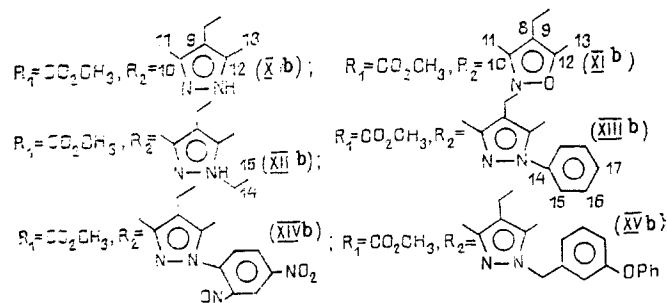
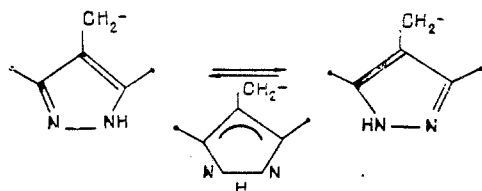


Table 1 gives the ^{13}C NMR spectral parameters of all the compounds that we studied. The spectrum of compound (I) contains the signals of the carbonyl carbon atoms of ketone group (203.93 ppm) and of the methoxycarbonyl (171.06 ppm) group, two doublet and singlet signals of the cyclopropane fragment showing a tetrasubstituted ring, and four quartets of methyl groups. Two quartets in weaker fields relate to methoxycarbonyl (51.83 ppm) and acetyl (32.05 ppm) groups and two in a stronger field to the gem-dimethyl group. The closeness of the signals of the latter (<1 ppm) show the 1,3-trans configuration of the substituents [5]. The 1,3-trans-configuration of the substituents in the ethoxycarbonyl derivative (IIa) were determined in just the same way.

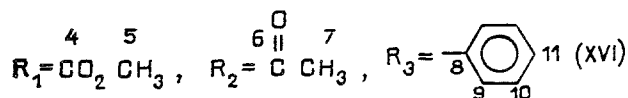
Conversely, in compound (III), the CS of the signal of the carbon atoms of the gem-dimethyl group differed by more than 14 ppm. This difference can be caused only by the cis-configuration of the substituents, in which one of the methyl groups (C-4) experiences two screening effects of steric nature, while the other (C-5) does not participate in interaction and, because of this, the signal is observed in the spectrum in a weaker field (28.88 ppm) than that of C-4 [5].

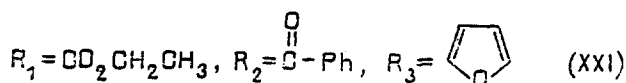
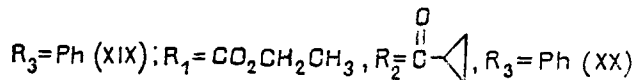
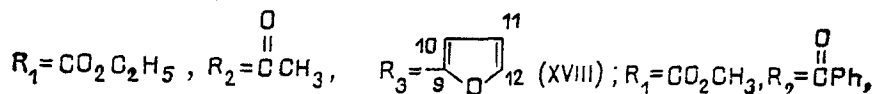
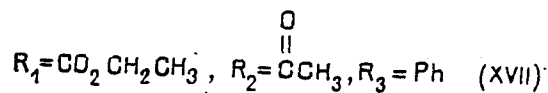
The appearance of a chiral center (C-9) in the substituent R_2 when one of the diastereotopic protons of the methylene group is brominated [compound (IVb)] leads to the formation of two diastereoisomers. Because of this, in the ^{13}C PMR spectrum there is a double set of signals. With the presence of a local plane of symmetry in substituent R_2 of compound (VI), the chiral center at C-9 disappears and in the spectrum a single set of signals is observed for the 1,3-cis isomer (b), just as in the case of compounds (VIIb-IXb).

In the case of each of the compounds with a nitrogen-containing substituent at C-8 (X-XV), there is a single 1,3-cis stereoisomer. In the spectrum of (Xb) there are only three signals for the dimethylpyrazole fragment, showing the symmetry of the fragments as the result of the delocalization of the multiple bonds, as shown in the scheme [7]:

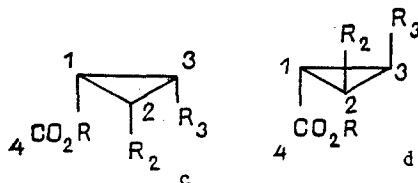


The replacement of the nitrogen atom by an oxygen atom in compound (XIb) or the introduction of a substituent at one of the nitrogen atoms of the pyrazole ring (XIIb-XVb) leads to a disturbance of the local axis of symmetry and to the appearance of all five nonequivalent signals (C-9-C-13).





More complicated for stereochemical analysis are compounds (XVI-XXI), each having three chiral centers in the cyclopropane fragment. For them, the formation of four diastereoisomers (a-d) is theoretically possible. However, the use of trans-enols as the starting material [9] led to the formation of only two stereoisomers in each case, with the given 1,2-trans configuration of two of the chiral centers (C-2 and C-3). In the ^{13}C NMR spectra of the compounds of the series investigated it is possible to observe that the signal of the carbonyl carbon atom, C-4, of the methoxycarbonyl group scarcely changes on passing from one isomer to the other. This fact confirms the formation of isomer of types a and b. In the case of isomers of types c and d, pronounced changes will be observed in the CS of the C-4 atom because of the different degrees of screening of the C=O carbon atom of the methoxycarbonyl group.



The assignment of the isomers within each pair of stereoisomers was based on the characteristic signals of the carbonyl group of R_2 and of the α -carbon atom of the substituent R_3 . Thus, in the isomeric pair (XVIa, b) the diamagnetic shifts of the C-6 signals in isomer (XVIa) and of C-8 in isomer (XVIb) showed 1,2-cis interaction in the former and 1,3-cis interaction in the latter case.

In the last group of tetrasubstituted cyclopropanes (XXII-XXV), again, the formation of four diastereoisomers (a-d) is possible. However, in reality only one isomer was isolated for each compound. A detailed analysis of the CSs of the α -atoms (the β -atoms for SMe) of the substituent showed that in isomer (a) for one of the ethoxycarbonyl and methylthio groups the shifts were practically independent of the structure of the aromatic fragment of the molecule. For the other, the 1,3-cis-oriented, ethoxycarbonyl group the C-4 signal was shifted from 169.39 (XXII) to 167.76 (XXIII) ppm, which showed a difference in the spatial interactions of these compounds. For the isomers (b-d) with a variation of the aromatic fragment changes in the CSs of the methylthio group and of an ethoxycarbonyl group (b), of the two ethoxycarbonyl groups (c), or only of the thiomethyl group (d) could have been expected, but no such changes were observed experimentally. This fact shows the preferential nature of the stereoisomer (a).

EXPERIMENTAL

The ^{13}C spectra were recorded on a JEOL FX-90Q spectrometer (22.5 MHz) with broadband and incomplete suppression of proton interactions. The field scan was 6024 Hz, and the resolution of the ADC was 0.75 Hz. CDCl_3 was used as the solvent with TMS as internal standard.

The synthesis of the compounds has been described in [8, 9].

TABLE 1. Parameters of the ^{13}C NMR Spectra of the Substituted Cyclopropanes (I)-(XXV) (δ , ppm, CDCl_3 , 25°C , 22.5 MHz)

Atom	Ia*	IIa*	III b	IVb, 9R*	IVb, 9S*	Vb, 9R*	Vb, 9S*
C-1	33,91 d	34,14 d	28,16 d	28,17 d	28,36 d	28,00 d	28,40 d
C-2	32,93 s	32,77 s	25,65 s	25,65 s	25,29 s	25,80 s	25,20 s
C-3	41,61 d	41,45 d	32,89 d	30,71 d	30,55 d	29,83 d	29,83 d
C-4	19,63 q	19,71 q	14,13 q	14,59 q	14,20 q	14,43 q	14,20 q
C-5	20,66 q	20,63 q	28,88 q	28,59 q	28,59 q	28,72 d	28,72 q
C-6	171,06 s	170,50 s	171,99 s	171,94 s	171,94 s	172,52 s	172,52 s
C-7	51,83 q	60,64 t	51,01 q	51,27 q	51,27 q	51,18 q	51,18 q
C-8	203,93 s	14,25 q	17,89 t	27,61 t	27,61 t	27,48 t	27,48 t
C-9	32,05 q	203,79 s	43,38 t	54,83 d	53,79 d	77,07 d	76,83 d
C-10		31,98 q	208,48 s	201,76 s	201,67 s	209,83 s	209,83 s
C-11			29,80 q	26,34 q	26,34 q	25,20 q	25,20 q

Atom	VI b	VII b	VIII b	IX b	X b	XI b
C-1	28,20 d	28,56 d	28,49 d	27,48 d	28,55 d	28,34 d
C-2	28,85 s	25,13 s	25,29 s	22,78 s	25,36 s	25,68 s
C-3	30,91 d	28,46 d	29,64 d	31,33 s	33,86 d	32,78 d
C-4	14,13 q	14,26 q	14,33 q	16,19 q	14,03 q	14,20 q
C-5	28,75 q	28,46 q	28,72 q	28,19 q	28,28 q	28,77 q
C-6	171,97 s	171,84 s	171,84 s	134,60 d	171,86 s	171,91 s
C-7	51,27 q	51,1 t	51,21 q	89,04 s	50,61 q	51,09 q
C-8	22,32 t	29,64 t	30,09 t	32,90 t	16,58 t	16,15 t
C-9	68,12 d	80,32 s	74,42 s	74,42 s	114,21 s	112,91 s
C-10	204,31 s	200,56 s	200,27 s	200,14 s	141,41 s	159,56 s
C-11	29,54 q	26,34 q	26,96 q	27,02 q	10,67 q	11,05 q
C-12	204,51 s	200,69 s	200,56 s	200,14 s	141,41 s	164,65 s
C-13	29,54 q	26,34 q	26,96 q	27,02 q	10,67 q	10,46 q

Atom	XII b	XIII b*	XIV b***	XV****	XVIa*	XVIIb*
C-1	28,55 d	28,60 d	28,49 d	28,46 d	31,76 d	31,59 d
C-2	25,74 s	25,79 s	25,85 s	25,65 s	37,63 d	34,66 d
C-3	30,34 d	34,08 d	33,36 d	34,14 d	33,32 d	33,19 d
C-4	14,36 q	14,41 q	14,33 q	14,36 q	169,39 s	168,94 s
C-5	28,93 q	28,99 q	28,85 q	28,85 q	52,22 q	51,86 q
C-6	172,45 s	172,24 s	172,13 s	172,07 s	202,55 s	204,80 s
C-7	50,58 q	51,09 q	51,14 q	50,92 q	30,81 q	31,80 q
C-8	17,31 t	17,45 t	17,36 t	17,36 t	127,77 s	134,34 s
C-9	115,48 s	117,41 s	119,72 s	116,19 s	126,32 d	128,17 d
C-10	135,10 s	136,26 s	137,51 s	136,04 s	128,63 d	128,63 d
C-11	12,16 q	12,30 q	12,16 q	12,34 q	127,18 d	127,29 d
C-12	145,45 s	147,81 s	45,86 s	146,15 s		
C-13	9,48 q	11,11 q	10,48 q	9,67 q		
C-14	43,51 t			52,29 t		
C-15	15,58 q					

Atom	XVIIa*	XVIIb*	XVIIIa*	XVIIIb*	XIXa*	XIXb*
C-1	32,05 d	31,76 d	30,42 d	30,68 d	29,58 d	29,51 d
C-2	37,86 d	34,53 d	35,22 d	82,83 d	35,05 d	34,89 d
C-3	30,29 d	32,96 d	23,24 d	26,44 d	31,66 d	32,08 d
C-4	169,07 s	168,71 s	107,78 s	168,02 s	168,96 s	168,51 s
C-5	61,30 t	60,77 t	60,81 t	61,80 t	61,16 t	60,77 t
C-6	14,23 q	13,97 q	14,03 q	14,07 q	14,00 q	14,00 q
C-7	202,62 s	204,77 s	200,66 s	203,83 s	193,44 s	196,31 s
C-8	30,94 q	31,07 q	29,90 q	30,94 q	138,03 s	138,16 s
C-9	138,00 s	134,97 s	150,82 s	148,09 s	128,27 d	128,27 d
C-10	126,57 d	128,67 d	106,27 d	107,97 d	128,64 d	128,69 d
C-11	128,72 d	128,96 d	110,48 d	110,51 d	132,69 d	133,39 d
C-12	127,22 d	127,22 d	140,90 d	141,78 d	138,03 s	134,82 s
C-13					126,53 d	128,14 d
C-14					128,53 d	128,86 d
C-15					127,02 d	127,22 d

TABLE 1 (continued)

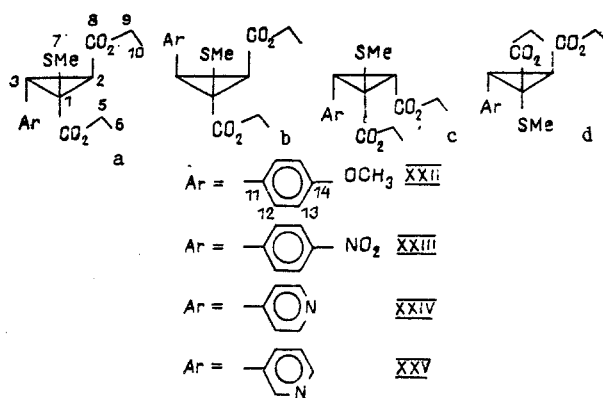
Atom	XXa*	XXb*	XXIa*	XXIb*	XXIIa	XXIIa	XXIV a	XXVa
C-1	31,99 d	31,76 d	30,03 d	30,88 d	42,21 s	42,46 s	42,30 s	42,10 s
C-2	37,76 d	34,50 d	32,96 d	29,64 d	34,32 d	34,51 d	33,91 d	34,24 d
C-3	28,89 d	32,70 d	23,14 d	29,93 d	36,25 d	36,23 d	35,58 d	33,74 d
C-4	168,77 s	168,51 s	168,41 s	168,41 s	169,39 s	167,76 s	167,83 s	168,02 s
C-5	61,07 t	60,67 t	61,13 t	61,13 t	61,36 t	62,11 t	62,08 t	62,01 t
C-6	14,20 q	14,00 q	14,10 q	14,10 q	14,17 q	14,13 q	14,13 q	14,17 q
C-7	202,88 s	206,99 s	193,26 s	195,79 s	15,09 q	15,18 q	15,05 q	15,08 q
C-8	21,97 d	21,77 d	133,33 s	136,79 s	168,55 s	168,61 s	168,67 s	168,83 s
C-9	10,90 t	11,45 t	128,43 d	128,43 d	61,74 t	61,76 t	61,72 q	61,69 t
C-10	11,16 t	11,35 t	128,76 d	128,76 d	14,17 q	14,13 q	14,13 q	14,17 q
C-11	138,16 s	134,66 s	133,59 d	133,59 d	12,67 s	168,79 s	142,80 d	129,67 s
C-12	126,41 d	128,07 d	151,13 s	143,19 s	129,87 d	129,73 d	123,93 d	156,33 d
C-13	128,56 d	128,89 d	108,00 d	108,00 d	113,51 d	123,21 d	149,45 d	128,73 d
C-14	126,97 d	127,16 d	110,54 d	110,54 d	158,96 s	141,39 s		122,81 d
C-15			141,42 d	141,78 d	55,24 q			135,91 d

*Figures published in [8].

**CS for the phenyl group: C_i - 139.95 s, C_o - 124.78 d, C_m - 128.89 d, C_p - 127.09 d.

***C-14) 151.57 s, C-15) 138.06 s, C-16) 127.29 d, C-17) 137.51 s, C-18) 129.21 d, C-19) 120.96 d.

****C-15) 139.76 s, C-16) 116.78 d, C-17) 156.86, C-18) 117.43 d, C-19) 129.90 d, C-20) 121.09 d, C-21) 157.58 s, C-22) 118.87 d, C-23) 129.64 d, C-24) 123.24 d.



SUMMARY

The ¹³C NMR spectra of 25 new substituted cyclopropanes of the pyrethroid series have been investigated and a stereochemical assignment has been made of the stereoisomers formed. As the criterion for stereochemical assignment it is proposed to use the values of the chemical shifts for the α-carbon atoms of the substituents in the cyclopropane ring.

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PHEROMONES OF INSECTS AND THEIR ANALOGS.

XX. METHYL-BRANCHED PHEROMONES BASED ON 4-METHYLTETRAHYDROPYRAN.

I. SYNTHESIS OF RACEMIC 4,8-DIMETHYLDECANAL - THE PHEROMONE OF THE FLOUR BEETLES *Tribolium confusum* AND *Tribolium castaneum*

V. N. Odinkov, G. Yu. Izhmuratov,
R. Ya. Kharisov, A. G. Ibragimov,
R. M. Sultanov, U. M. Dzhemilev,
and G. A. Tolstikov

UDC 547.3+632.78

A synthesis is proposed of 4,8-dimethyldecanal (VIII) - a pheromone of the flour beetles *Tribolium confusum* and *T. castaneum*. By heating 71.2 g of 4-methyltetrahydropyran (I), 83.2 g of AcBr and 1.57 g of ZnCl₂ (45°C), then 120°C, 2 h), 1-acetoxy-5-bromo-3-methylpentane (II) was obtained. The hydrolysis of 19.8 g of (II) (MeOH-H₂O, TsOH, 20°C, 15 h) gave 5-bromo-3-methylpentan-1-ol (III). From 18.1 g of (III) and 38.9 ml of 2,3-dihydropyran (Et₂O, TsOH, 20°C, 20 h) was obtained the 2-THPL ester of (III), (IV), which was converted into 3-methyloct-7-en-1-ol (V) by the treatment of the corresponding Grignard reagent with allyl bromide (THF, CuI-bi-2-pyridyl, 2°C, 4 h, Ar). The interaction of 1.42 g of (V) with Et₃Al (hexane, 20°C, Cp₂ZrCl₂, Ar) gave 3,7-dimethylnonan-1-ol (VI), boiling which with 48% HBr in the presence of concentrated H₂SO₄ gave 1-bromo-3,7-dimethylnonane (VII) which was then converted into the desired (VIII) by the reaction of the corresponding Grignard reagent with DMFA (0-2°C, 1 h; 20°C, 2 h; Ar). The characteristics of the compounds - yield (%), n_D (°C): (I), 79, 1.4340 (22); (III) 89, 1.4660 (23); (IV), 82, 1.4739 (23); (V), 85, -; (VI), 90, 1.4483 (20); (VII), 88, 1.4409 (22); (VIII), 88, 1.4589 (22). Details of the IR and PMR spectra of compounds (II)-(VII) are given.

Racemic 4,8-dimethyldecanal, which possesses attractant activity in relation to the flour beetles *Tribolium confusum* and *T. castaneum* [1] has been obtained previously from citronellal [2, 3], methyl cyclopropyl ketone [4], and the cyclic dimer of isoprene [5].

Broad possibilities for the synthesis of methyl-branched pheromones are opened up by the use of synthons of α,ω-bifunctional 3-methylpentanes - products of the cleavage of the readily available 4-methyltetrahydropyran (I) [6]. Thus, the reactions of compound (I) with acetyl bromide in the presence of zinc chloride led to 1-acetoxy-5-bromo-3-methylpentane (II), which was converted into 1-bromo-3-methyl-5-(tetrahydropyran-2-yl)pentane (IV) via the bromohydrin (III). The 1,5-dimethyl-branched carbon skeleton of the desired pheromone was constructed by the carboalumination of the terminally unsaturated alcohol (V) obtained by the coupling of the bromide (IV) with allyl bromide by means of the Grignard reaction. The carboalumination reaction catalyzed by dicyclopentadienylzirconium

Institute of Chemistry, Bashkir Scientific Center, Urals Branch, USSR Academy of Sciences, Ufa. Translated from Khimiya Prirodnikh Soedinenii, No. 2, pp. 272-276, March-April, 1989. Original article submitted May 23, 1988; revision submitted September 22, 1988.