Absolute Configuration of the Pyrethrins. Configuration and Structure of (+)-Allethronyl (+)-*trans*-Chrysanthemate 6-Bromo-2,4-dinitrophenylhydrazone by *X*-Ray Methods

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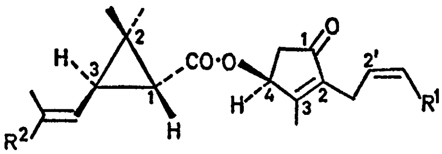
Summary The six natural pyrethrins (II)—(VII) and (+)-allethronyl (+)-*trans*-chrysanthemate (VIII) have the same absolute configurations (o.r.d. and c.d.) at C-4; *X*-ray structure determination of the title derivative shows this to be 4(*S*) and provides conformational information.

Natural pyrethrins[1] (II)—(VII) have highly desirable insecticidal properties. Meaningful structure-activity analysis[2] requires secure stereochemical assignments. The absolute configuration of the cyclopropane part of the esters, (+)-*trans*-chrysanthemic acid and (+)-*trans*-pyrethric acid, was determined chemically,[3]† but information on the ketols is sparse. Oxidation of (+)-pyrethrolone methyl ether $[\alpha]_D^{26}$ + 10·5° (ethanol) is reported[4] to give (−)-α-methoxysuccinic acid $[\alpha]_D^{27}$ − 25·0° (acetone) [optical purity



(I)

(II)	Pyrethrin I	(I), R^1 = CH:CH$_2$,R^2 = Me
(III)	» II	(I), R^1 = CH:CH$_2$, R^2 = CO$_2$Me
(IV)	Cinerin I	(I), R^1 = R^2 = Me
(V)	» II	(I), R^1 = Me, R^2 = CO$_2$Me
(VI)	Jasmolin I	(I), R^1 = Et, R^2 = Me
(VII)	» II	(I), R^1 = Et, R^2 = CO$_2$Me
(VIII)	(+)-Allethronyl (+)-*trans*-chrysanthemate	(I), R^1 = H, R^2 = Me

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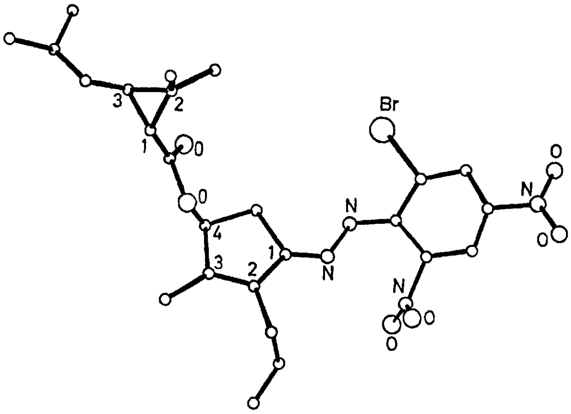
† Crystallographic analysis of natural (+)-*trans*-chrysanthemic acid as its *p*-bromophenacyl ester confirms the chemical results. (Personal communication, Professor G. Ferguson).

ca. 43%, the pure acid[5] of known (*S*) absolute configuration having $[\alpha]^{13}_{D}$ $-58{\cdot}2°$, in acetone] but subsequent work[6] has shown pure (+)-pyrethrolone methyl ether to have $[\alpha]^{20}_{D}$ + 99° (methanol). The isolation of a degradation product of *ca.* 43% optical purity from (+)-pyrethrolone methyl ether of only about 10·6% optical purity is unexplained, unless solvent change from ethanol to methanol has drastic rotational effects: we have re-examined the problem by crystallographic means.

Comparison of the o.r.d. and c.d. curves for all six natural pyrethrin esters shows that they are all of the same configuration at C-4 of the ketol (positive c.d. max. at 316 nm). The synthetic rethrin (VIII), formed by esterification of (+)-allethrolone with (+)-*trans*-chrysanthemic acid, also belongs to the identical stereochemical series (o.r.d. and c.d.). The 6-bromo-2,4-dinitrophenylhydrazone of (VIII), $C_{25}H_{29}N_4O_6Br$ was prepared. The monoclinic crystals (space group $P2_1$) had $a = 9{\cdot}84$, $b = 7{\cdot}72$, $c = 19{\cdot}78$ Å; $\beta = 105{\cdot}00°$, $Z = 2$. Intensity data were collected with Mo-K_α radiation and **614** independent reflections were considered observed. Patterson synthesis located the bromine positions and the remaining 35 non-hydrogen atoms were found by Fourier methods. The structure was refined by least squares (block-diagonal) to an R-index of 8·85% using isotropic temperature factors, except for bromine (anisotropic factors). The Figure shows the resulting structure which, using the known 1(*R*)-, 3(*R*)-configuration of the cyclopropane system, gives a 4(*S*)-configuration for the ketol. This result accords with further work in which the absolute configuration of the derivative of (VIII) was determined by anomalous dispersion: the difference between the two enantiomers was significant at the 0·025 level.[7] Further confirmation came from independent measurement of Bijvoet pairs of reflexions. Twenty-two pairs were compared, for which F_c differed by more than 10%, and for which observed intensities were significantly different: twenty-one pairs supported the assigned absolute configuration. Rethrin (VIII) is thus prop-2′-enyl-4(*S*)-rethronyl-1(*R*),3(*R*)-chrysanthemate. It follows that the natural rethrins (II)—(VII) have identical absolute configurations.‡



FIGURE

The 2″-nitro-group of the derivative employed is twisted out of the plane of the benzene ring by steric interactions, and the crystallographic structure shows various conformational features which may prove of interest in structure-activity analysis of the pyrethrins.

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‡ Applying Feldman notation for generating stereonumbers, as discussed earlier,[1] natural (II) is 8-pyrethrin I and natural (III) is 17-pyrethrin II.

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