# Absolute Configuration of (+)-*trans*-Chrysanthemic Acid. Crystal Structure Analysis of a *p*-Bromoanilide Derivative

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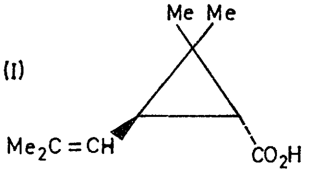
The absolute configuration of (+)-*trans*-chrysanthemic acid, deduced previously from chemical considerations as 1*R*,2*R* has been confirmed by a three-dimensional *X*-ray analysis of a *p*-bromoanilide derivative using Bijvoet's anomalous dispersion method. Crystals are orthorhombic, space group $P2_12_12_1$, with $Z = 4$ in a unit cell of dimensions $a = 9.58(2)$, $b = 6.06(2)$, $c = 27.53(5)$ Å. The structure was solved from photographic data by the heavy-atom method, and refined by least-squares calculations to *R* 0.109 for 400 reflexions.

THE chemistry of the natural pyrethrins has been the subject of considerable interest[1] and the absolute configuration of a key compound in pyrethrin chemistry, (+)-*trans*-chrysanthemic acid, (I), has been deduced as 1*R*,2*R* from chemical considerations.[2] Because of its importance in a number of reactions[3] we undertook an *X*-ray determination of the absolute configuration of (+)-*trans*-chrysanthemic acid by use of a *p*-bromoanilide derivative.

(I)



## EXPERIMENTAL

*Crystal Data.*—$C_{16}H_{20}NOBr$, $M = 322$. Orthorhombic, $a = 9.58(2)$, $b = 6.06(2)$, $c = 27.53(5)$ Å, $U = 1.602$ Å$^3$, $D_m = 1.33$ g cm$^{-3}$, $Z = 4$, $D_c = 1.34$ g cm$^{-3}$, $F(000) = 664$. Space group $P2_12_12_1$ ($D_2^4$, No. 19), uniquely from systematic absences. Cu-$K_\alpha$ *X*-radiation, $\lambda = 1.542$ Å; $\mu$(Cu-$K_\alpha$) = 37.9 cm$^{-1}$.

*Crystallographic Measurements.*—A crystal was mounted about the *a* axis and the unit-cell parameters were determined from Weissenberg photographs taken with Cu-$K_\alpha$ radiation and from precession photographs taken with Mo-$K_\alpha$ ($\lambda = 0.7107$ Å) radiation. Equi-inclination Weissenberg photographs of the 0—4*kl* reciprocal lattice nets yielded some 400 independent reflexions, which proved to be sufficient for the determination of the structure and the absolute configuration. Intensities were estimated visually by comparison with a calibrated step-wedge and were corrected for the appropriate Lorentz and polarisation factors. The various sets of structure amplitudes were placed on an approximate absolute scale at a later stage in the analysis.

*Structure Determination.*—The position of the bromine atom (0,0.187,0.210) was found by Patterson methods. The initial (heavy-atom-phased) electron-density distribution was inevitably complicated by the presence of pseudo-mirror symmetry resulting from the bromine *x* co-ordinate being zero. Nevertheless, by careful selection of atomic sites from this distribution the entire structure was revealed and two further cycles of structure-factor and electron-density calculations lowered *R* to 0.29. In these calculations an overall isotropic thermal parameter, $U_{iso}$ 0.06 Å$^3$ was used, along with the atomic scattering factors given in ref. 4. Structure amplitudes were placed on an approximate absolute scale by making $k\Sigma|F_o| = \Sigma|F_c|$ for each layer.

*Structure Refinement.*—Seven cycles of least-squares calculations reduced *R* to its final value of 0.109. In the last two cycles bromine was refined anisotropically and carbon, nitrogen, and oxygen isotropically. A weighting scheme of the form: $\sqrt{w} = \{[1 - \exp(-p_1 \sin\theta/\lambda)^2]/(1 + p_2|F_o| + p_3|F_o|^2)\}^{1/2}$ was used in the calculations and the *p* parameters were adjusted during refinement to their final values of $p_1 = 50$, $p_2 = 0.0001$, $p_3 = 0.001$. Final fractional co-ordinates, thermal parameters, and their estimated standard deviations are listed in Table 1. Interatomic distances and angles calculated from the co-ordinates of Table 1 are in Table 2. A view of the molecule down *a* and our numbering scheme is shown in Figure 1, and the arrangement of the molecule in the unit cell in Figure 2.

TABLE 1

Fractional co-ordinates (Br × $10^4$, others × $10^3$) and isotropic thermal parameters (Å$^2$ × $10^3$), with estimated standard deviations in parentheses

| Atom | *x* | *y* | *z* | $U_{iso}$ |
|---|---|---|---|---|
| Br | −0 079(8) | 1 809(9) | 2 103(2) | * |
| C(1) | 139(5) | −455(6) | −052(1) | 064(1) |
| C(2) | 104(5) | −669(6) | −072(1) | 065(1) |
| C(3) | 053(5) | −476(6) | −097(1) | 080(1) |
| C(4) | 110(5) | −405(7) | −141(1) | 083(1) |
| C(5) | 049(5) | −290(6) | −175(1) | 077(1) |
| C(6) | 113(5) | −198(7) | −220(1) | 099(1) |
| C(7) | −107(5) | −166(8) | −167(1) | 109(1) |
| C(8) | 238(6) | −812(9) | −093(1) | 114(2) |
| C(9) | 001(6) | −830(6) | −045(1) | 085(1) |
| C(10) | 082(8) | −375(8) | −012(2) | 061(2) |
| C(11) | 112(4) | −175(6) | 066(1) | 056(1) |
| C(12) | 037(5) | −274(5) | 098(1) | 061(1) |
| C(13) | −016(6) | −179(6) | 142(1) | 085(1) |
| C(14) | 046(5) | 030(6) | 154(1) | 065(1) |
| C(15) | 129(5) | 144(6) | 120(1) | 070(1) |
| C(16) | 165(5) | 033(6) | 077(1) | 078(1) |
| N | 156(4) | −276(4) | 024(1) | 064(1) |
| O | −054(4) | −379(4) | 000(1) | 053(1) |

* Anisotropic thermal parameters in the form: $\exp[-2\pi^2(0.16h^2a^{*2} + 0.13k^2b^{*2} + 0.12l^2c^{*2} - 0.05klb^*c^* - 0.02lhc^*a^* + 0.03hka^*b^*)]$.

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[1] L. Crombie and M. Elliott, *Fortschr. Chem. org. Naturstoffe*, XIX, ed. L. Zechmeister, Springer Verlag Ven, 1961, p. 120, and references therein.

[2] L. Crombie and S. H. Harper, *J. Chem. Soc.*, 1954, 470.

[3] See *e.g.* L. Crombie, R. P. Houghton, and D. K. Woods, *Tetrahedron Letters*, 1967, 4553.

[4] 'International Tables for *X*-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

Structure amplitudes and final structure factors are listed in Supplementary Publication No. SUP 21414 (6 pp., 1 microfiche), together with anomalous dispersion inequalities.

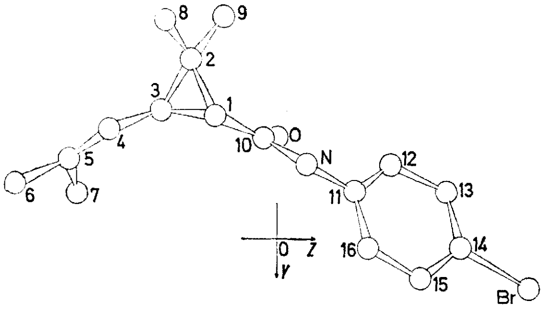

FIGURE 1 A view of the molecule down the *a* axis, showing our numbering scheme

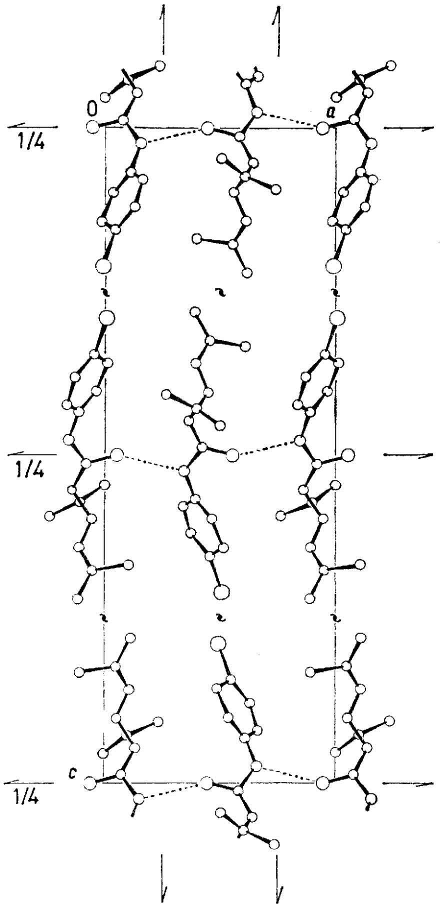

FIGURE 2 The arrangement of the molecules in the unit cell. The N–H · · · O bond is broken

DISCUSSION

The restricted number of data in the $x$ direction has, not unexpectedly, led to poor resolution in that direction, which can in this instance be ignored since the sole object of the analysis was the determination of the absolute configuration of the molecule. After due consideration of the estimated standard deviations none of the bond lengths and angles differ significantly from those listed in ref. 5 and in view of the limited accuracy little would be gained by dwelling upon them in detail.

The absolute configuration was established by Bijvoet's anomalous dispersion method.[6] Structure-factors calculated for $F_c(hkl)$ and $F_c(\bar{h}\bar{k}\bar{l})$ were compared with the corresponding intensities (indexed in a right-handed system). Of 33 pairs only 4 had inequalities opposite to those of the observed structure factors. The co-ordinates of Table 1 and Figures 1 and 2 thus represent the absolute configuration of the molecule which is identical with that deduced from the chemical work.[2] The molecules of the derivative are maximally extended in the crystal and are held by a spiral system of C=O · · · H–N (O · · · N 3.00 Å) hydrogen bonds about a two-fold screw-axis (Figure 2). All other intermolecular distances correspond to, or are larger than, van der Waals distances.

TABLE 2

(*a*) Interatomic distances (Å) and angles (°) *

| | | | |
|---|---|---|---|
| C(1)–C(2) | 1.45(5) | C(10)–O | 1.34(8) |
| C(1)–C(3) | 1.49(5) | C(10)–N | 1.34(6) |
| C(1)–C(10) | 1.33(6) | C(11)–C(12) | 1.28(5) |
| C(2)–C(3) | 1.44(5) | C(11)–C(16) | 1.39(5) |
| C(2)–C(8) | 1.65(7) | C(11)–N | 1.39(4) |
| C(2)–C(9) | 1.57(6) | C(12)–C(13) | 1.44(5) |
| C(3)–C(4) | 1.40(5) | C(13)–C(14) | 1.43(5) |
| C(4)–C(5) | 1.31(6) | C(14)–C(15) | 1.39(5) |
| C(5)–C(6) | 1.48(5) | C(14)–Br | 1.88(3) |
| C(5)–C(7) | 1.69(7) | C(15)–C(16) | 1.41(5) |

(*b*) Bond angles

| | | | |
|---|---|---|---|
| C(2)–C(1)–C(3) | 59(2) | C(6)–C(5)–C(7) | 108(3) |
| C(2)–C(1)–C(10) | 123(4) | C(1)–C(10)–N | 123(6) |
| C(3)–C(1)–C(10) | 120(5) | C(1)–C(10)–O | 126(5) |
| C(1)–C(2)–C(3) | 62(3) | N–C(10)–O | 110(4) |
| C(1)–C(2)–C(8) | 115(4) | C(10)–N–C(11) | 130(4) |
| C(1)–C(2)–C(9) | 122(3) | C(12)–C(11)–C(16) | 119(3) |
| C(3)–C(2)–C(8) | 122(3) | C(12)–C(11)–N | 123(3) |
| C(3)–C(2)–C(9) | 121(4) | C(16)–C(11)–N | 118(3) |
| C(8)–C(2)–C(9) | 109(3) | C(11)–C(12)–C(13) | 126(3) |
| C(1)–C(3)–C(2) | 59(3) | C(12)–C(13)–C(14) | 113(4) |
| C(1)–C(3)–C(4) | 118(4) | C(13)–C(14)–C(15) | 122(3) |
| C(2)–C(3)–C(4) | 123(4) | C(13)–C(14)–Br | 120(3) |
| C(3)–C(4)–C(5) | 127(5) | C(15)–C(14)–Br | 117(3) |
| C(4)–C(5)–C(6) | 127(5) | C(14)–C(15)–C(16) | 117(3) |
| C(4)–C(5)–C(7) | 123(3) | C(15)–C(16)–C(11) | 121(4) |

(*c*) Hydrogen bonded atoms †

| | |
|---|---|
| $N \cdots O^{I}$ | 3.00(7) Å |

* Mean σ in bond lengths 0.05 Å, and bond angles 4°. † The superscript I refers to equivalent position $\frac{1}{2} + x, -\frac{1}{2} - y, -z$.

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[6] J. M. Bijvoet, *Proc., k. ned Akad. Wetenschap*, 1949, **52**, 313.