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## Crystal Structure of ( $\pm$ )-Methyl 2-[4-(2,4-Dichlorophenoxy)phenoxy]propionate, a New Selective Grass Herbicide of the Phenoxy-Phenoxy Series

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The crystal structure of the selective phenoxy-phenoxy grass herbicide ( $\pm$ )-methyl 2-[4-(2,4-dichlorophenoxy)phenoxy]propionate (Diclofop-methyl) has been determined by direct methods and refined by least squares to a final residual of 0.039 for 1297 observed reflections. The conformational features of the 2-phenoxypropionate moiety in the molecule closely resemble those of the substituted 2-phenoxypropionic acid herbicides, where structural aspects are well systematized. There appears to be little conformational change associated with the presence of the substituent methyl ester group on the acid.

The title compound, ( $\pm$ )-methyl 2-[4-(2,4-dichlorophenoxy)phenoxy]propionate (compound HOE 23 408; proposed common name Diclofop-methyl) is the first commercial member of a new series of phenoxy-phenoxy herbicides developed from 1971 onward by Hoechst AG, Frankfurt-Main, Germany) (Nestler et al., 1979). It has also been shown that the (+) enantiomer is the herbicidally active species (Nestler and Bieringer, 1980). Now marketed under the trade names Illoxan, Hoelon, and Hoe-Grass, this compound (along with other members of the series) has specific herbicidal properties, quite unlike those of the synthetic auxin compounds of the 2,4-D type, in particular, the 2-propionic acids such as Dichloroprop, Silvex, and Mecoprop. Optimum activity in the series is attained in Diclofop-methyl, being remarkably effective against grassy-type weeds such as wild oats and millet, which constitute a serious pest problem in commercial crops, e.g., wheat, barley, sugar beet, and soybeans. It is tolerant toward many monocotyledons and dicotyledons. Just as with the phenoxyalkanoic acid series, activity is found in both the free acid salts and esters.

Development of the series involved a comparison of likely compounds variously substituted in the second aromatic ring with the inactive unsubstituted parent compound. This was done by using the Topliss operational scheme for aromatic substitution (Topliss, 1972). In this circumstance it was of interest to compare the solid-state structure of Diclofop-methyl with those of the phenoxy acid analogues. Altogether structural and conformational aspects of 20 phenoxyalkanoic acids have been determined by using X-ray diffraction techniques (Table I). Two

reviews of the structural trends of these acids (Smith and Kennard, 1979; Kennard et al., 1981a) indicate that the preferred conformation of the acetic acid analogues is one with the gross molecule planar, whereas for 2-propionic acids, the  $\alpha$ -substituted methyl group tends to lie in the appropriate molecular plane with the oxo acid side chain in a perpendicular orientation. This is found in two commercial propionic acid herbicides whose structures have been determined [Silvex (Smith et al., 1977); Mecoprop (Smith et al., 1980)]. Furthermore, these acids are chemical analogues of compounds having hypolipidaemic properties, e.g., 2-[4-(4-chlorophenoxy)phenoxy]propionic acid (Schacht, 1977). An investigation of the structural systematics of this series has now been initiated (Kennard et al., 1981a).

### EXPERIMENTAL SECTION

**Crystal Data.**  $C_{16}H_{14}Cl_2O_4$ ;  $M_r = 341.2$ ; monoclinic; space group  $P2_1/c$ ;  $a = 13.968$  (5) Å,  $b = 12.561$  (6) Å,  $c = 9.247$  (5) Å;  $\beta = 98.74$  (4)° (cell parameters and their standard deviations were obtained from 12 high-angle reflections by using the Syntex system);  $V = 1603$  Å<sup>3</sup>;  $Z = 4$ ;  $D_{\text{calcd}} = 1.41$  g cm<sup>-3</sup>;  $F(000) = 704$ ;  $\mu(\text{Mo K}\alpha) = 4.04$  cm<sup>-1</sup>.

**Data Collection, Structure Solution, and Refinement.** Crystals suitable for X-ray analysis were obtained by recrystallization from hexane of the sample of HOE 23 408 provided by Hoechst Aktiengesellschaft, Frankfurt. A total of 1297 reflections with  $I > 2.5\sigma(I)$  were considered observed out of 2025 collected in a unique set from a crystal (0.22 × 0.13 × 0.35 mm) mounted about the  $c$  axis on a Syntex  $P2_1$  four-circle diffractometer ( $2\theta_{\text{max}} = 45^\circ$ ) by using graphite crystal monochromated Mo  $K\alpha$  radiation ( $\lambda = 0.7107$  Å). No corrections were made for absorption [ $\mu(\text{Mo K}\alpha) = 4.04$  cm<sup>-1</sup>].

The structure was solved by using MULTAN (Germain et al., 1971). Full-matrix least-squares refinement with anisotropic thermal parameters for all nonhydrogen atoms reduced  $R$  [ $=\sum||F_o - F_c||/\sum|F_o|$ ] to 0.039 and  $R_w$

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Table I. Phenoxyalkanoic Acid Structures Determined by X-ray Methods

acid	reference
2,4-dichlorophenoxyacetic acid (2,4-D)	Smith and Kennard (1979) <sup>a</sup>
2,5-dichlorophenoxyacetic acid (2,5-D)	Smith and Kennard (1979) <sup>a</sup>
2,4,5-trichlorophenoxyacetic acid (2,4,5-T)	Smith and Kennard (1979) <sup>a</sup>
2,4,6-trichlorophenoxyacetic acid (2,4,6-T)	Smith and Kennard (1979) <sup>a</sup>
2-(3,5-dichlorophenoxy)propionic acid (3,5-DP)	Smith and Kennard (1979) <sup>a</sup>
2-(2,4,5-trichlorophenoxy)propionic acid (2,4,5-TP; Silvex)	Smith and Kennard (1979) <sup>a</sup>
2-(4-chloro-2-methylphenoxy)propionic acid (MCCPP; Mecoprop)	Smith et al. (1980)
2-(2-chlorophenoxy)propionic acid (OCPA)	Smith et al. (1981a)
bis(2-chlorophenoxy)acetic acid	Smith and Kennard (1981a)
bis(4-chlorophenoxy)acetic acid	Smith and Kennard (1981a)
4-chloro-2-methylphenoxyacetic acid (MCPA)	Smith and Kennard (1981b)
4-chlorophenoxyacetic acid (PCPA)	Kennard et al. (1981c)
2-chlorophenoxyacetic acid (OCPA) (redetermination)	Kennard and Smith (1981)
3,4-dichlorophenoxyacetic acid (3,4-D)	Smith et al. (1981b)
phenoxyacetic acid	Kennard et al. (1981a)
2-phenoxypropionic acid	Kennard et al. (1981a)
2-(4-chlorophenoxy)propionic acid (PCPP)	Kennard et al. (1981a)
2-methyl-2-phenoxypropionic acid	Kennard et al. (1981a)
2-methyl-2-(4-chlorophenoxy)propionic acid (clofibric acid)	Kennard et al. (1981a)
2-(4-chlorophenoxy)-2-phenylpropionic acid	Kennard et al. (1981b)
2-chlorophenoxyacetic acid (OCPA)	Chandrasekhar and Patabhi (1977)
4-ethylphenoxyacetic acid	Galdecki and Kozłowska (1978)
4-nitrophenoxyacetic acid	Kumar and Rao (1980)
2-methyl-2-[4-(4-chlorophenoxy)phenoxy]propionic acid	Wagner and Malmros (1979)

<sup>a</sup> Also references cited therein.

Table II. Atomic Coordinates (H,  $\times 10^3$ ; others,  $\times 10^4$ ) and H Isotope Thermal Parameters ( $A^2$ ,  $\times 10^2$ ) with Estimated Standard Deviations (in Parentheses)

	x	y	z		x	y	z	U
C(1)	9730 (2)	1623 (2)	4842 (3)	H(2)	935 (2)	59 (3)	313 (4)	6 (1)
C(2)	9918 (3)	922 (3)	3773 (4)	H(3)	1095 (2)	24 (3)	280 (4)	7 (1)
C(3)	10853 (3)	710 (3)	3574 (4)	H(5)	1190 (2)	221 (2)	619 (3)	5 (1)
C(4)	11600 (3)	1192 (3)	4449 (4)	H(6)	1036 (2)	253 (2)	649 (4)	5 (1)
C(5)	11433 (3)	1869 (3)	5553 (4)	H(43)	1548 (3)	155 (3)	617 (4)	8 (1)
C(6)	10480 (3)	2095 (3)	5747 (4)	H(45)	1405 (2)	-60 (3)	803 (4)	6 (1)
C(41)	13288 (3)	855 (3)	5223 (4)	H(46)	1262 (3)	-21 (3)	625 (4)	10 (1)
C(42)	14137 (3)	1389 (3)	5163 (4)	H(8)	884 (2)	254 (2)	679 (3)	22 (1)
Cl(42)	14205 (1)	2337 (1)	3843 (2)	H(81A)	699 (3)	235 (3)	507 (4)	7 (1)
C(43)	14941 (3)	1172 (4)	6171 (5)	H(81B)	735 (3)	161 (3)	637 (4)	7 (1)
C(44)	14888 (3)	440 (3)	7241 (4)	H(81C)	721 (3)	284 (3)	669 (4)	9 (1)
Cl(44)	15910 (1)	196 (2)	8515 (1)	H(11A)	902 (4)	569 (4)	564 (6)	14 (2)
C(45)	14041 (3)	-100 (4)	7316 (5)	H(11B)	802 (3)	557 (3)	437 (5)	9 (2)
C(46)	13245 (3)	114 (3)	6314 (4)	H(11C)	795 (3)	597 (4)	605 (5)	11 (2)
O(4)	12535 (2)	1036 (3)	4116 (3)					
O(7)	8757 (2)	1764 (2)	4908 (2)					
C(8)	8454 (3)	2571 (3)	5814 (4)					
C(81)	7430 (3)	2317 (4)	6008 (6)					
C(9)	8551 (2)	3654 (2)	5124 (3)					
O(10)	8901 (2)	3819 (2)	4049 (3)					
O(11)	8181 (2)	4408 (2)	5886 (2)					
C(11)	8280 (4)	5498 (3)	5390 (6)					

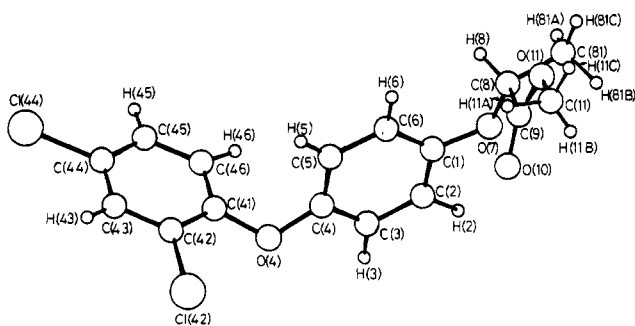


Figure 1. Molecular configuration and atom numbering scheme for Diclofop-methyl viewed perpendicular to C(41)-O(4)-C(4).

$[=\sum w(|F_o - F_c|)^2 / \sum (w|F_o|^2)^{1/2}]$  to 0.049. The value of  $w$  used in the weighting scheme was  $1.0 / (\sigma^2 F_o + 5 \times 10^{-4} F_o^2)$ . Hydrogen positions were located in a difference-Fourier synthesis and included in the refinement with their positional and isotropic thermal parameters ( $U$ ) fixed.

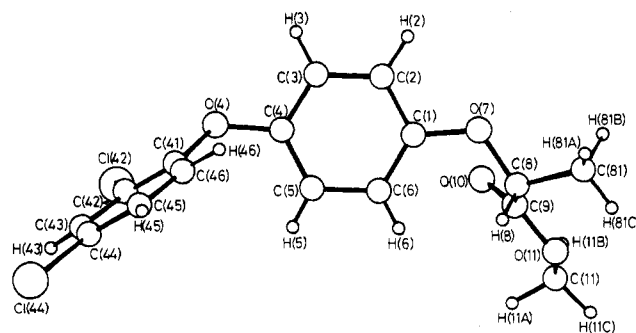


Figure 2. View perpendicular to the plane of the primary phenoxy group.

A final difference Fourier synthesis revealed no significant features. No corrections were made for extinction. Atomic scattering factors were those of Cromer and Mann (1968) for nonhydrogens and of Stewart et al. (1965) for hydrogen. Positional parameters are listed in Table II and

Table III. Anisotropic Thermal Parameters ( $\text{\AA}^2, \times 10^3$ ) with Estimated Standard Deviations<sup>a</sup>

	$U_{11}$	$U_{22}$	$U_{33}$	$U_{12}$	$U_{13}$	$U_{23}$
C(1)	42 (2)	31 (2)	47 (2)	-2 (2)	3 (2)	8 (2)
C(2)	54 (2)	37 (2)	39 (2)	4 (2)	5 (2)	4 (2)
C(3)	71 (3)	53 (2)	37 (2)	11 (2)	10 (2)	8 (2)
C(4)	51 (2)	65 (3)	51 (2)	17 (2)	21 (2)	15 (2)
C(5)	42 (2)	61 (3)	62 (3)	-5 (2)	-4 (2)	-5 (2)
C(6)	47 (2)	47 (2)	61 (3)	2 (2)	8 (2)	-11 (2)
C(41)	46 (2)	59 (2)	60 (2)	13 (2)	20 (2)	3 (2)
C(42)	63 (3)	52 (2)	79 (3)	-4 (2)	32 (2)	3 (2)
Cl(42)	155 (1)	100 (1)	146 (1)	-10 (1)	66 (1)	50 (1)
C(43)	55 (3)	80 (3)	94 (3)	-23 (3)	32 (3)	-22 (3)
C(44)	43 (2)	95 (3)	62 (2)	6 (2)	4 (2)	20 (2)
Cl(44)	61 (1)	222 (2)	96 (1)	25 (1)	-12 (1)	-24 (1)
C(45)	63 (3)	66 (3)	64 (3)	3 (2)	12 (2)	10 (2)
C(46)	47 (3)	67 (3)	66 (3)	-9 (2)	10 (2)	3 (2)
O(4)	54 (2)	146 (3)	58 (2)	29 (2)	20 (2)	21 (2)
O(7)	40 (1)	43 (1)	65 (2)	-1 (1)	6 (1)	-10 (1)
C(8)	47 (2)	41 (2)	48 (2)	4 (2)	8 (2)	2 (2)
C(81)	53 (3)	63 (3)	84 (4)	-7 (2)	21 (3)	2 (3)
C(9)	38 (2)	49 (2)	43 (2)	4 (2)	-6 (2)	3 (2)
O(10)	100 (2)	57 (2)	64 (2)	11 (2)	37 (2)	13 (1)
O(11)	72 (2)	42 (1)	54 (1)	9 (1)	15 (1)	1 (1)
C(11)	97 (4)	41 (2)	81 (4)	10 (3)	5 (3)	-2 (2)

<sup>a</sup> Temperature factors are of the form  $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^{*}b^{*} + 2U_{13}hla^{*}c^{*} + 2U_{23}klb^{*}c^{*})]$ .

Table IV. Bond Distances ( $\text{\AA}$ ) and Angles (Deg) with Estimated Standard Deviations

(a) Distances			
C(1)-C(2)	1.379 (5)	C(8)-C(9)	1.517 (5)
C(1)-C(6)	1.372 (5)	C(9)-O(10)	1.191 (4)
C(1)-O(7)	1.381 (4)	C(9)-O(11)	1.331 (4)
C(2)-C(3)	1.372 (6)	O(11)-C(11)	1.457 (5)
C(3)-C(4)	1.361 (5)	C(2)-H(2)	1.00 (3)
C(4)-C(5)	1.376 (6)	C(3)-H(3)	0.95 (4)
C(4)-O(4)	1.400 (5)	C(5)-H(5)	0.92 (3)
C(5)-C(6)	1.400 (6)	C(6)-H(6)	0.91 (3)
C(41)-O(4)	1.371 (4)	C(43)-H(43)	0.89 (4)
C(41)-C(42)	1.371 (5)	C(45)-H(45)	0.91 (3)
C(42)-C(43)	1.373 (6)	C(46)-H(46)	0.96 (4)
C(42)-Cl(42)	1.718 (4)	C(8)-H(8)	0.98 (3)
C(43)-C(44)	1.361 (6)	C(81)-H(81A)	0.98 (4)
C(44)-C(45)	1.375 (6)	C(81)-H(81B)	0.96 (4)
C(44)-Cl(44)	1.735 (4)	C(81)-H(81C)	0.99 (4)
C(45)-C(46)	1.362 (5)	C(11)-H(11A)	1.05 (6)
C(46)-C(41)	1.381 (5)	C(11)-H(11B)	0.96 (4)
C(8)-O(7)	1.420 (4)	C(11)-H(11C)	1.01 (5)
C(8)-C(81)	1.503 (6)		
(b) Angles			
C(2)-C(1)-O(7)	114.2 (3)	C(43)-C(44)-C(45)	120.9 (4)
C(2)-C(1)-C(6)	120.1 (3)	C(43)-C(44)-Cl(44)	118.9 (3)
C(6)-C(1)-O(7)	125.6 (3)	C(45)-C(44)-Cl(44)	120.3 (3)
C(1)-C(2)-C(3)	120.6 (3)	C(44)-C(45)-C(46)	119.2 (4)
C(2)-C(3)-C(4)	119.6 (3)	C(45)-C(46)-C(41)	120.6 (4)
C(3)-C(4)-C(5)	121.0 (4)	C(46)-C(41)-C(42)	119.6 (3)
C(3)-C(4)-O(4)	117.6 (3)	C(46)-C(41)-O(4)	122.9 (3)
C(5)-C(4)-O(4)	121.3 (3)	C(1)-O(7)-C(8)	120.1 (2)
C(4)-C(5)-C(6)	119.5 (4)	O(7)-C(8)-C(9)	109.7 (3)
C(5)-C(6)-C(1)	119.1 (4)	O(7)-C(8)-C(81)	107.7 (3)
C(4)-O(4)-C(41)	119.6 (3)	C(81)-C(8)-C(9)	112.8 (3)
O(4)-C(41)-C(42)	117.3 (3)	C(8)-C(9)-O(10)	125.5 (3)
C(41)-C(42)-C(43)	119.9 (4)	C(8)-C(9)-O(11)	110.4 (3)
C(41)-C(42)-Cl(42)	120.6 (3)	O(10)-C(9)-O(11)	124.1 (3)
C(43)-C(42)-Cl(42)	119.5 (3)	C(9)-O(11)-C(11)	116.0 (3)
C(42)-C(43)-C(44)	119.9 (4)		

Table V. Torsion Angles (Degrees) about Bonds in Diclofop-methyl

C(3)-C(4)-O(4)-C(41)	-138.1	C(1)-O(7)-C(8)-C(81)	-163.2
C(4)-O(4)-C(41)-C(42)	-135.9	O(7)-C(8)-C(9)-O(11)	+173.9
C(2)-C(1)-O(7)-C(8)	-171.2	C(8)-C(9)-O(11)-C(11)	+176.4
C(1)-O(7)-C(8)-C(9)	+74.0		

anisotropic thermal parameters in Table III, while bond distances and angles are given in Table IV. Lists of ob-

served and calculated structure factor amplitudes are deposited as supplementary material (see paragraph at end

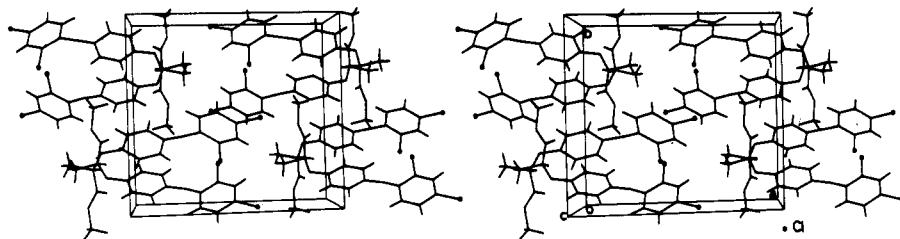


Figure 3. Stereoview of the cell contents perpendicular to the *ab* plane.

of paper regarding supplementary material).

#### DISCUSSION

The atom numbering scheme and molecular conformation for Diclofop-methyl are shown in Figures 1 and 2 and follow the convention used for members of the phenoxyalkanoic acid series (Smith and Kennard, 1979). The 2,4-dichlorophenoxy part of the molecule is similar in its distance and angular parameters to the equivalent part of 2,4-D (Smith et al., 1976). This includes the distortion of the exo ring angles about C(41) [122.9°, 117.3 (3)°]. The magnitude of this distortion is not as great as that for C(1) in the primary phenoxy group of the molecule [125.6°, 114.2 (3)°] but similar to those for 2,4-D [124.7°, 116.2 (3)°]. This is understandable in terms of the greater degree of steric crowding provided by the oxopropionic ester group. Comparable distortions caused by opening of angles away from the  $\alpha$ -methyl or the  $\alpha$ -methyl substituent group occur without exception among the phenoxyalkanoic acid analogues with the mean values for 22 acids being 124.6° and 115.2°, respectively. The preferred conformation of the phenoxypropionic acid with the  $\alpha$ -methyl group lying in the approximate plane of the primary phenoxy residue is also found in this example. The oxoacetic acid group and its methyl substituent, which are approximately coplanar, are thus oriented perpendicular to the phenoxy group with the carbonyl oxygen [O(10)] at a distance of 2.717 (4) Å from the ether oxygen [O(7)]. This distance is predictable considering the structural systematics of members of the phenoxyacetic and 2-phenoxypropionic acid series (Table I) where the range and mean are 2.605–2.775 and 2.711 Å, respectively. A consequence of this is the *synplanar-synplanar* (carbonyl) side-chain conformation, found without exception among the same group of compounds. A listing of all significant torsion angles about bonds in the molecule is given in Table V.

The angles between plane 1, containing atoms C(1), C(2), C(3), C(4), C(5), and C(6), plane 2, containing atoms C(41), C(42), C(43), C(44), C(45), and C(46), and plane 3, containing atoms C(8), C(9), O(10), and O(11), are 81.9° for planes 1 and 2 and 78.0° for planes 1 and 3.

The presence of the methyl ester group on O(11) does not appear to influence greatly the gross molecular conformation compared with those for the free acids, where cyclic hydrogen-bonded dimers are usual. However, the packing mode in the unit cell for this ester is very different (Figure 3) compared to those found for normal free acids. The molecules form discrete noninteracting units with no significant intermolecular contacts. Biological activity would appear to be dependent structurally on the secondary effects related to the nature and disposition of the substituent groups in the para-substituted phenoxy group since it is similar to 2-(4-chlorophenoxy)propionic acid (Kennard et al., 1981a). This suggests that the title com-

pound cannot act as an auxin particularly if the conformational change theory for auxin action is to operate (Kaethner, 1977; Katekar, 1979).

**Supplementary Material Available:** Lists of observed and calculated structure factor amplitudes (6 pages). Ordering information is given on any current masthead page.

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