Review Article

Crystal Packing and Supramolecular Motifs in Four Phenoxyalkanoic Acid Herbicides—Low-Temperature Redeterminations

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A low-temperature redetermination by X-ray crystallography of four phenoxyalkanoic acid herbicides, 4-chloro-2-methylphenoxyacetic acid (MCPA), *rac*-2-(4-chloro-2-methylphenoxy)propionic acid (MCP), 2,4-dichlorophenoxyacetic acid (2,4-D), and 2,4-dichlorophenoxybutyric acid (2,4-DB), allowed the supramolecular structures of these compounds to be precisely described in terms of C···O/C–H··· π interactions. The geometric parameters of the redetermined structures agree with those previously reported, but with improved precision.

1. Introduction

Phenoxyalkanoic acids, having methyl and/or chlorine substituent groups in the *ortho* and *meta* positions of the benzene ring, are known selective herbicides, used to control broadleaf weeds in crop production. The first compound of this group, used already in 1944 in agriculture for weed control, was 2,4-dichlorophenoxyacetic acid (2,4-D). The physico- and biological properties of this group of compounds have been the subject of extensive studies [1–3]. As part of our wider study on metal complexes with herbicides of the phenoxyalkanoic acid series and on the herbicide-soil-plant interaction [4, 5], we report here structure redeterminations at 90 K of 4-chloro-2-methylphenoxyacetic acid (C₉H₉ClO₃; MCPA; compound **1**), *rac*-2-(4-chloro-2-methylphenoxy)propionic acid (C₁₀H₁₁ClO₃; MCP; compound **2**), 2,4-dichlorophenoxyacetic acid (C₈H₆Cl₂O₃; 2,4-D; compound **3**), and 2,4-dichlorophenoxybutyric acid (C₁₀H₁₀Cl₂O₃; 2,4-DB; compound **4**). The structures of the compounds **1**–**3** were determined using X-ray diffraction data [6–9], collected at ambient temperature many years ago, with inaccurate refined or missing hydrogen atoms. The structure of **4** was previously determined at 173 K. In result,

weak hydrogen interactions could not be precisely defined, and supramolecular structures have not been fully analyzed. These kind of bonds have been found to play an important role in many biological structures, as proteins, polypeptides, and drug-binding interactions [10–12].

2. Experimental

Structures of the compounds **1**–**4** were determined by using single-crystal X-ray diffraction methods, using the Bruker AXS Smart APEX-II CCD 3-circle diffractometer with MonoCap capillary and monochromated Mo K α radiation (λ = 0.71073 Å, 50 kV, 32 mA) at 90 K. Data collection and data reduction were done with the SMART [13] and SAINT-PLUS [14] programs. All structures were solved by direct methods and refined by the full-matrix least-squares methods on F² with anisotropic thermal for all nonhydrogen atoms. All hydrogen atoms were located in difference Fourier syntheses and were refined freely. The final geometrical calculations were carried out using the PLATON program [15]. The relevant crystal data and experimental details are summarized in Table 1. Figures were drawn using Mercury [16] and SHELXTL [14] programs.

TABLE 1: Crystal data and structural refinement details for compounds 1–4.

	1	2	3	4
Empirical formula	C ₉ H ₉ ClO ₃	C ₁₀ H ₁₁ ClO ₃	C ₈ H ₆ Cl ₂ O ₃	C ₁₀ H ₁₀ Cl ₂ O ₃
Formula weight	200.61	214.64	221.03	249.08
Crystal system	Triclinic	Monoclinic	Triclinic	Triclinic
Space group	<i>P</i> −1	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> −1	<i>P</i> −1
<i>a</i> (Å)	5.0867 (3)	4.2261 (3)	7.1246 (2)	7.4845 (4)
<i>b</i> (Å)	7.7824 (4)	6.8196 (5)	7.8399 (2)	8.7892 (5)
<i>c</i> (Å)	12.2134 (7)	35.176 (3)	8.8991 (3)	9.3777 (4)
α (°)	73.933 (1)	90	90.654 (1)	81.0720 (14)
β (°)	84.610 (2)	91.801 (2)	104.565 (1)	69.5538 (13)
γ (°)	77.009 (1)	90	110.527 (1)	65.3163 (12)
<i>V</i> (Å ³), <i>Z</i>	452.45 (4), 2	1013.28 (13), 4	447.82 (2), 2	525.18 (5), 2
<i>d</i> _{calc} (g/cm ³)	1.472	1.407	1.639	1.575
<i>F</i> (000)	208	448	224	256
Temperature (K)	90	90	90	90
Radiation type, wavelength (Å)	Mo K α , 0.71073	Mo K α , 0.71073	Mo K α , 0.71073	Mo K α , 0.71073
Absorption coeff. (mm ^{−1})	0.391	0.354	0.692	0.600
Theta range (°)	1.7–27.0	2.3–25.0	2.4–27.0	2.3–27.0
Limiting indices, <i>h</i> , <i>k</i> , <i>l</i>	−6 → 6, −9 → 9, −15 → 15	−5 → 5, −8 → 8, −41 → 41	−9 → 9, −10 → 10, −11 → 11	−9 → 9, −11 → 11, −11 → 11
Reflections collected	9864	17135	9777	11607
Unique reflections	1974 [<i>R</i> _{int} = 0.0233]	1756 [<i>R</i> _{int} = 0.0208]	1928 [<i>R</i> _{int} = 0.0148]	2287 [<i>R</i> _{int} = 0.0148]
Completeness to $\theta_{\max}$	99.7%	99.7%	99.2%	99.6%
Data/Restraints/Parameters	1974/0/154	1756/0/171	1928/0/143	2287/0/176
Goodness-of-fit on <i>F</i> ²	1.13	1.27	1.07	1.03
Final <i>R</i> indices [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> = 0.0308, <i>wR</i> ² = 0.0860	<i>R</i> = 0.0347, <i>wR</i> ² = 0.0811	<i>R</i> = 0.0199, <i>wR</i> ² = 0.0523	<i>R</i> = 0.0206, <i>wR</i> ² = 0.0583
Final <i>R</i> indices [all data]	<i>R</i> = 0.0316, <i>wR</i> ² = 0.0864	<i>R</i> = 0.0349, <i>wR</i> ² = 0.0812	<i>R</i> = 0.0201, <i>wR</i> ² = 0.0525	<i>R</i> = 0.0209, <i>wR</i> ² = 0.0585
Largest diff. peak and hole (e [−] Å ^{−3})	0.398, −0.272	0.274, −0.228	0.407, −0.193	0.404, −0.217

Compound 1: weight = $1/[\sigma^2(F_0^2) + (0.0418P)^2 + 0.2516P]$, where $P = (\max(F_0^2, 0) + 2 F_c^2)/3$,
 Compound 2: weight = $1/[\sigma^2(F_0^2) + (0.0189P)^2 + 1.0828P]$, where $P = (\max(F_0^2, 0) + 2 F_c^2)/3$,
 Compound 3: weight = $1/[\sigma^2(F_0^2) + (0.0235P)^2 + 0.2140P]$, where $P = (\max(F_0^2, 0) + 2 F_c^2)/3$,
 Compound 4: weight = $1/[\sigma^2(F_0^2) + (0.0329P)^2 + 0.2198P]$, where $P = (\max(F_0^2, 0) + 2 F_c^2)/3$.

3. Results

The unit-cell dimensions and atomic coordinates show that the phase is the same at both 90 K and ambient temperature for all redetermined structures. All described molecules associate *via* strong head-to-head carboxyl O–H...O hydrogen bonds, forming typical carboxylic acid cyclic dimers about centres of symmetry into *R*₂²(8) rings [17, 18]. The compounds also crystallize with one independent molecule in the asymmetric unit.

The oxoacetic acid side chain in compound 1 adopts an extended planar conformation, with a C1–O3–C7–C8 torsion angle of 170.89(12)° (Figure 1).

Apart for the strong head-to-head hydrogen-bonded ring motif common to carboxylic acids [O1–H1...O2^{−x−1,−y+2,−z}], the molecules are also connected into

dimers, forming 14-membered rings *via* C6–H6...O1^{−x,−y+1,−z} interactions with symmetry-related molecules. The close contact between the Cl4 and the aryl methyl C9 group [Cl4...C9^{1+x,−1+y,z} = 3.412(2) Å] is also observed (Figure 2). All three types of interactions are mutually coplanar and parallel to a crystallographic (1 1 −2) plane. A methylene group participates in a C7–H71... π interaction, with a benzene ring of an adjacent layer, and these serve to connect polymeric planes into a three-dimensional network.

In the structure of compound 2, the side chain C1–O3–C7–C8 torsion angle of 84.6(2)° indicates a synclinal conformation of the chain (Figure 3).

The main intermolecular interactions are the *R*₂²(8) dimers involving strong hydrogen bonds O1–H1...O2^{−x+1,−y,−z} between the carboxyl groups of adjacent molecules. Another hydrogen-bonding interaction involves

FIGURE 1: A molecular diagram of **1**, showing the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

FIGURE 2: A fragment of the structure of **1**, showing the two-dimensional polymeric framework formed through the intermolecular O–H...O hydrogen bonds and C–H...O and C–Cl...C contacts, shown as dashed lines.

FIGURE 3: A molecular diagram of **2**, showing the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

a methine H7 atom that is engaged in bifurcated symmetrical C7–H7...O contacts to carboxyl O1 and ether O3 atoms of neighbouring molecule, and making a graph-set motif of $C_1^2(3)[R_1^2(5)]$, running along *a* axis (Figure 4). A bifurcation is confirmed by the sum of angles about atom H7, which is $359.7(10)^\circ$ [19].

Replacement of the 2-methyl ring substituent group in **1** by a chlorine atom in **3** results in a different conformation

FIGURE 4: The molecular packing of the compound **2**, showing atoms of a neighbouring molecule, making a $C_1^2(3)[R_1^2(5)]$ graph set motif, running along the *a* axis. Dashed lines indicate the hydrogen-bonding interactions. All the hydrogens except for the methine H7 have been removed for clarity.

FIGURE 5: A molecular diagram of **3**, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

FIGURE 6: The molecular packing of the compound **3**, showing the alternating $R_2^2(6)$ and $R_2^2(8)$ rings, running along the *b* axis. Dashed lines indicate the hydrogen-bonding interactions. All the hydrogens except H71 and H72 have been removed for clarity.

of the chain that is synclinal, with a C1–O3–C7–C8 torsion angle of $81.02(13)^\circ$ (Figure 5).

A methylene group is engaged here in two relatively strong C–H...O interactions with carboxyl O1 and ether O3 atoms, forming in effect two centrosymmetric $R_2^2(6)$ and $R_2^2(8)$ rings (Figure 6). The C3–H3...O2^{−x+1,−y+1,−z+1} contact and its symmetry-related counterpart join two another molecules, generating an $R_2^2(14)$ graph-set motif. The

FIGURE 7: A molecular diagram of **4**, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

FIGURE 8: The intermolecular O-H...O, C-H...O, C-H... π and Cl...Cl contacts in compound **4**, shown as dashed lines. All the hydrogens except those not involved in interactions have been removed for clarity.

structure shows also a significant contact between adjacent benzene rings with a centroid separation distance of 3.6505(7) Å, and the C2-Cl2...Cg 1^{1-x,1-y,1-z} [Cg1 is the centroid of ring C(1-6)] contact with a Cl... π separation of 3.5610(6) Å.

Compound **4** is conformationally similar to **1** and adopts the planar conformation, confirmed by the torsion angles of C1-O3-C7-C8 = 179.20(10), O3-C7-C8-C9 = -178.25(9), and C7-C8-C9-C10 = 173.83(11)° (Figure 7).

The neighbouring molecules are connected *via* O1-H1...O2^{-x+1,-y-1,-z+2}, C5-H5...O2^{x-1,y+1,z}, C6-H6...O1^{-x,-y,-z+2} hydrogen bonds and a short Cl2...Cl2^{1-x,-y,-z} nonbonding interaction of 3.2976(4) Å which are mutually coplanar and parallel to crystallographic plane (2 2 1). Further interactions in the crystal structure of C7-H71...Cl4^{-x,-y+1,-z+1}, C8-H81...O3^{-x+1,-y,-z+1} and C8-H82...Cg 1^{-x,-y,-z+1} [Cg1 is the centroid of ring C(1-6)] connect adjacent polymeric layers into a three-dimensional supramolecular network (Figure 8).

The comparison of the all analyzed structures shows that the C2-Cl2 bond lengths of 1.7323(11) and 1.7371(10)° in **3** and **4** are distinctly shorter than C4-Cl4, ranging from 1.7416(11) to 1.746(2)° in **1-4**. The bond lengths in the carboxylic acid group range from 1.2171(13) to 1.2211(18) Å

TABLE 2: Selected bond lengths (Å) and angles (°) for compounds **1-4**.

1	
Cl4-C4	1.746 (2)
O1-C8	1.313 (2)
O2-C8	1.219 (2)
O3-C1	1.385 (2)
O3-C7	1.418 (2)
C1-O3-C7-C8	84.6 (2)
O3-C7-C8-O1	177.84 (15)
2	
Cl4-C4	1.746 (2)
O1-C8	1.313 (2)
O2-C8	1.219 (2)
O3-C1	1.385 (2)
O3-C7	1.418 (2)
C1-O3-C7-C8	84.6 (2)
O3-C7-C8-O1	177.84 (15)
3	
Cl2-C2	1.7323 (11)
Cl4-C4	1.7416 (11)
O1-C8	1.3194 (13)
O2-C8	1.2183 (15)
O3-C1	1.3677 (13)
O3-C7	1.4157 (13)
C1-O3-C7-C8	81.02 (13)
O3-C7-C8-O1	-179.94 (9)
4	
Cl2-C2	1.7371 (10)
Cl4-C4	1.7443 (11)
O1-C10	1.3250 (13)
O2-C10	1.2171 (13)
O3-C1	1.3584 (13)
O3-C7	1.4393 (12)
C1-O3-C7-C8	179.20 (10)
O3-C7-C8-C9	-178.25 (10)
C7-C8-C9-C10	173.83 (11)
C8-C9-C10-O1	-169.26 (11)

and from 1.313(2) to 1.3250(13) Å for C=O and C-OH, respectively. Selected bond distances and torsion angles are listed in Table 2. Hydrogen-bonding geometries are listed in Table 3.

4. Conclusion

A low-temperature redetermination by X-ray crystallography of four phenoxyalkanoic acids have been carried out. Investigations of the interactions shown the typical carboxylic acid cyclic O-H...O hydrogen bonds between adjacent molecules. However, their conformations and molecular packing in the crystals are quite different, which can be

TABLE 3: Close contacts of hydrogen bond type [$\text{\AA}$ and $^\circ$] for compounds 1–4.

D–H...A	D–H	H...A	D...A	D–H...A
1				
O1–H1...O2 ⁱ	0.82 (2)	1.81 (2)	2.6342 (15)	178 (3)
C6–H6...O1 ⁱⁱ	0.90 (2)	2.56 (2)	3.4253 (19)	161.6 (19)
C7–H71...Cg1 ⁱⁱⁱ	0.98 (2)	2.66 (2)	3.4207 (16)	134.4 (13)
2				
O1–H1...O2 ^{iv}	0.82 (3)	1.83 (3)	2.645 (2)	176 (3)
C7–H7...O2 ^v	0.97 (2)	2.72 (2)	3.474 (2)	135.6 (14)
C7–H7...O3 ^v	0.97 (2)	2.71 (2)	3.647 (2)	164.0 (15)
3				
O1–H1...O2 ^{vi}	0.82 (2)	1.81 (2)	2.6330 (13)	178.2 (13)
C3–H3...O2 ^{vii}	0.95 (2)	2.54 (2)	3.4335 (14)	157.2 (13)
C7–H71...O3 ^{viii}	0.94 (1)	2.47 (1)	3.2454 (14)	140.0 (12)
C7–H72...O1 ^{iv}	0.97 (2)	2.54 (2)	3.5073 (15)	173.0 (12)
4				
O1–H1...O2 ^{ix}	0.81 (2)	1.85 (2)	2.6578 (12)	172.4 (18)
C5–H5...O2 ^x	0.93 (1)	2.72 (1)	3.4078 (13)	131.0 (11)
C6–H6...O1 ^{xi}	0.96 (2)	2.74 (2)	3.6937 (13)	179.4 (14)
C7–H71...Cl4 ^{xii}	0.99 (2)	2.89 (2)	3.7830 (14)	151.3 (12)
C8–H81...O3 ^{xiii}	0.97 (1)	2.78 (2)	3.7390 (13)	176.4 (11)
C8–H82...Cg1 ^{xiv}	0.98 (2)	2.70 (2)	3.5369 (13)	143.5 (12)

Cg1 = centroid C(1–6).

Symmetry codes: ⁱ $x-1, -y+2, -z$; ⁱⁱ $x, -y+1, -z$; ⁱⁱⁱ $x-1, y, z$; ^{iv} $x+1, -y, -z$; ^v $x+1, y, z$; ^{vi} $x, -y, -z$; ^{vii} $x+1, -y+1, -z+1$; ^{viii} $x+1, -y+1, -z$; ^{ix} $x+1, -y-1, -z+2$; ^x $x-1, y+1, z$; ^{xi} $x, -y, -z+2$; ^{xii} $x, -y+1, -z+1$; ^{xiii} $x+1, -y, -z+1$; ^{xiv} $x, -y, -z+1$.

explained by the influence of significant C–H...O, C–H... π , C–Cl...C intermolecular contacts, forming supra-molecular structures. The additional contacts of the π ... π and C–Cl... π type have been observed in compound 3, and the Cl...Cl type in compound 4.

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