

The Structure of the New Insect-Growth Regulator 1,4-Bis(5-chloropent-4-ynyloxy)benzene

BY J. C. J. BART, I. W. BASSI, M. CALCATERA AND P. PICCARDI

Montedison 'G. Donegani' Research Institute, Via G. Fauser 4, Novara, Italy

(Received 6 June 1979; accepted 3 March 1980)

Abstract

The structure of the new insect-growth regulator 1,4-bis(5-chloropent-4-ynyloxy)benzene, $C_{16}H_{16}Cl_2O_2$, has been determined from 602 diffractometer data. Crystals are monoclinic, space group $P2_1/n$, $a = 4.691$ (2), $b = 28.68$ (1), $c = 6.018$ (4) Å, $\beta = 102.20$ (5)°, $V = 791.5$ Å³, $Z = 2$, $d_c = 1.30$, $d_o = 1.32$ Mg m⁻³. The structure was solved by direct methods and refined by least-squares methods to $R = 0.073$. The O—C(α)—C(β) side chains of the alkoxy groups adopt a coplanar arrangement with the phenyl ring, leading to extensive in-plane bond-angle distortions at the *ipso* C atoms. The low melting point of the compound is explained in terms of molecular packing.

Introduction

The title compound, $C_6H_4[O(CH_2)_3C\equiv CCl]_2$, is a new, potent insect-growth regulator with juvenile hormone activity. The ability of this compound to interfere with the metamorphosis of the larvae and pupae of many insect species of the families Lepidoptera, Coleoptera and Homoptera has been extensively studied (Bettarini, Massardo, Piccardi & Longoni, 1978). The compound differs significantly in structure from the well known terpenoid insect-growth regulators (Sláma, Romaňuk & Šorm, 1974) and yet retains some of their important biological manifestations. The crystal structure investigation of the new juvenile hormone analogue was undertaken as part of a study to understand better its mechanism of action.

Experimental

1,4-Bis(5-chloropent-4-ynyloxy)benzene, (I), was recrystallized from an acetone–methanol mixture; preliminary cell parameters and the space group were obtained from Weissenberg photographs. Using a small crystal mounted on a Picker FACS-I four-circle computer-controlled diffractometer equipped with a

scintillation counter and a pulse-height analyser, accurate cell dimensions and an orientation matrix were derived by a least-squares fit of the χ , φ , ω and 2θ values from 12 independent reflexions.

Crystal data

$C_{16}H_{16}Cl_2O_2$, $M_r = 311.22$, monoclinic, $a = 4.691$ (2), $b = 28.68$ (1), $c = 6.018$ (4) Å, $\beta = 102.20$ (5)°, $V = 791.5$ Å³, $Z = 2$; $d_o = 1.32$, $d_c = 1.30$ Mg m⁻³, m.p. 335 K. Space group $P2_1/n$ from systematic absences: $0k0$ for k odd, $h0l$ for $h + l$ odd.

Intensity measurements were made with a colourless crystal $0.25 \times 0.4 \times 0.8$ mm mounted with c parallel to the φ axis of the diffractometer using Ni-filtered $Cu K\alpha$ radiation ($\lambda = 1.54178$ Å) up to $2\theta = 120^\circ$. The moving-crystal–moving-counter technique was used with a 2θ scan rate of 1° min^{-1} and a scan range of 2.0 – 2.5° in order to account properly for the separation of the $K\alpha_1$ and $K\alpha_2$ peaks at various 2θ values. Background counts of 10s were measured at each end of every 2θ scan. During the data collection three standards were measured before every 50 reflections. Of the 1178 independent reflexions measured, 602 were considered observed and had $I > 2.5\sigma$ $\{\sigma = [N_s + (t_s/t_b)^2 N_b]^{1/2}$, where N_s is the total peak count during the time of scanning t_s , and t_b is the time spent in measuring the N_b background counts}. An arbitrary intensity equal to 0.5 times the observable limit was assigned to the non-observed reflexions. All intensities were corrected for Lorentz and polarization effects and for absorption as $\mu(Cu K\alpha) = 3.786 \text{ mm}^{-1}$.

The structure was solved by means of the multi-resolution tangent-refinement method *MULTAN* (Germain, Main & Woolfson, 1971). The positions of all non-hydrogen atoms were obtained from a Fourier map phased with the information derived from the application of *MULTAN*. The positional and isotropic thermal parameters of these atoms were refined to $R = (\sum ||F_o| - |F_c||) / \sum |F_o| = 0.25$ by several cycles of block-diagonal least squares minimizing the function $\Delta = \sum w(|F_o| - |F_c|)^2$ according to the program of Immirzi (1967).

Table 1. Final fractional coordinates, with estimated standard deviations in parentheses

	x	y	z
Cl	0.2054 (5)	0.77772 (6)	-0.0003 (3)
O	-0.5743 (7)	0.94415 (11)	-0.7451 (5)
C(1)	-0.0045 (14)	0.81228 (119)	-0.1787 (10)
C(2)	-0.1675 (12)	0.83571 (18)	-0.3054 (9)
C(3)	-0.3741 (12)	0.86376 (18)	-0.4712 (9)
C(4)	-0.2439 (12)	0.88045 (18)	-0.6684 (9)
C(5)	-0.4658 (11)	0.90427 (17)	-0.8496 (8)
C(6)	-0.7836 (10)	0.97099 (15)	-0.8796 (8)
C(7)	-0.8847 (10)	1.00830 (16)	-0.7731 (7)
C(8)	-0.8996 (11)	0.96284 (16)	-1.1108 (8)
H(31)	-0.440	0.8945	-0.385
H(32)	-0.567	0.8433	-0.538
H(41)	-0.066	0.9050	-0.604
H(42)	-0.151	0.8506	-0.740
H(51)	-0.366	0.9156	-0.990
H(52)	-0.642	0.8803	-0.917
H(7)	-0.790	1.0150	-0.594
H(8)	-0.818	0.9334	-1.198

Atomic scattering factors were calculated from the expression given by Vand, Eiland & Pepinsky (1957) using the values for the parameters given by Moore (1963). The weighting scheme $1/w = A + B|F_o| + C|F_o|^2$ was adopted, according to Cruickshank, Pilling, Bujosa, Lovell & Truter (1961), where $A = 2F_o(\text{min.})$, $B = 1.0$ and $C = 2/F_o(\text{max.})$. After anisotropic refinement, the H atoms were introduced in the calculations at fixed positions with their coordinates defined on stereochemical grounds (C—H, 1.09 Å) and in agreement with a ΔF synthesis. The assumed B value for all H atoms was taken as 5.0 Å². Refinement then converged to $R = 0.073$ for the 602 non-zero reflexions. The final shifts of the atomic parameters were negligible and all well below the corresponding σ .

The final fractional coordinates and the corresponding standard deviations of the independent unit are listed in Table 1.* All calculations were performed on the Univac 1100/20 computer of this Institute using a local program set.

Results and discussion

The molecular and crystal structures of (I) are displayed in Figs. 1 and 2, as derived by ORTEP (Johnson, 1970). The bond lengths and angles with their e.s.d.'s are reported in Table 2; no corrections have been applied for thermal-motion effects. The overall symmetry of the molecule is C_i ($\bar{1}$), as imposed by space-group symmetry. The geometry of the

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35016 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

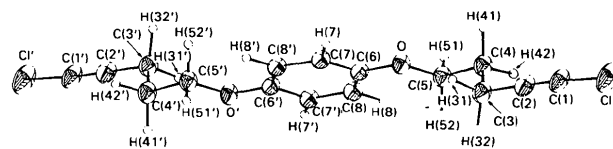


Fig. 1. The molecule of 1,4-bis(5-chloropent-4-ynyloxy)benzene, showing the atom-labelling scheme and 30% probability thermal-vibration ellipsoids.

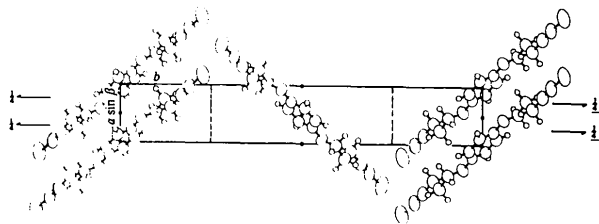


Fig. 2. Structure of 1,4-bis(5-chloropent-4-ynyloxy)benzene viewed down the c axis.

Table 2. Bond data of 1,4-bis(5-chloropent-4-ynyloxy)benzene

(a) Bond lengths (Å)			
Cl—C(1)	1.630 (7)	C(5)—O	1.449 (6)
C(1)—C(2)	1.171 (9)	O—C(6)	1.370 (6)
C(2)—C(3)	1.474 (8)	C(6)—C(7)	1.382 (6)
C(3)—C(4)	1.522 (7)	C(6)—C(8)	1.402 (7)
C(4)—C(5)	1.503 (8)	C(7)—C(8')	1.378 (7)
(b) Bond angles (°)			
Cl—C(1)—C(2)	176.5 (6)	O—C(6)—C(7)	115.8 (4)
C(1)—C(2)—C(3)	177.8 (6)	O—C(6)—C(8)	124.9 (4)
C(2)—C(3)—C(4)	112.6 (5)	C(6)—C(7)—C(8')	121.1 (3)
C(3)—C(4)—C(5)	112.2 (5)	C(6)—C(8)—C(7')	119.5 (4)
C(4)—C(5)—O	107.3 (4)	C(7)—C(6)—C(8)	119.3 (4)
C(5)—O—C(6)	117.5 (3)		

molecule is best described in terms of two planes through the extended aromatic system and (part of) the chain (Table 3) with an interplanar angle of 55.9°.

Bond lengths are in the expected ranges. The mean aromatic C—C distance of 1.387 (7) Å conforms to the value generally accepted for the C—C length (1.398 Å) in unsubstituted benzene (Colapietro & Domenicano, 1977, and references therein). The O—C(5) bond length of 1.449 (6) Å is at the limit for a normal paraffinic C—O bond distance [1.426 (5) Å; Sutton, 1965], whereas the shortening of the phenyl—O bond to 1.370 (6) Å is in agreement with the value of 1.367 Å found in a variety of alkoxybenzenes (Sletten, 1973, 1974, 1975; Ruban & Luger, 1975; Rabinovich & Schmidt, 1970; Rousseaux, Meunier-Piret, Putzeys, Germain & Van Meerssche, 1972; Hecht & Luger, 1974; van den Hark, Hendriks & Beurskens, 1974; van Koningsveld, 1973; Cotrait, Sy & Ptak, 1975; Bryan & Jenkins, 1975; Bryan & Fallon, 1975; Bryan &

Table 3. *Least-squares planes*

(a) Equations of best planes

The best planes, represented by the equation $lX + mY + nZ - p = 0$, are referred to the a^* , b , c orthogonal axis system.

Plane	l	m	n	p	r.m.s.d.(Å)
Ring	-0.7032	-0.5862	0.4024	0.0020	0.010
Chain	0.3757	0.8125	0.4457	0.9275	0.040

(b) Displacements (Å) of the atoms from the best planes

E.s.d.'s are 0.005, 0.012 and 0.012 Å for the Cl, O and C atoms, respectively. Asterisks denote atoms not defining the plane.

Ring		Chain	
O	0.012	Cl	-0.028
C(6)	-0.007	C(1)	0.030
C(6')	0.003	C(2)	0.028
C(7)	-0.010	C(3)	-0.028
C(7')	0.006	C(4)	-0.001
C(8)	-0.009		
C(8')	0.005		
C(5)	0.036*		
C(4)	0.071*		

Freyberg, 1975). The average $C(sp^3)-C(sp^3)$ single-bond length of 1.513 (8) Å is not significantly different from the standard value of 1.537 (5) Å, and the C(2)-C(3) distance of 1.474 (8) Å is in agreement with the reported average $C(sp^3)-C(sp)$ length of 1.459 (5) Å (Sutton, 1965) and within the range 1.416-1.48 Å for simple alkynes (Simonetta & Gavezzotti, 1978). Also, the triple-bond distance of 1.171 (9) Å is in accordance with the reported average X-ray value of 1.171 Å for simple alkynes (Simonetta & Gavezzotti, 1978). The C(1)-Cl bond length of 1.630 (7) Å agrees well with reported C(sp)-Cl distances of 1.635 (5) Å (Sutton, 1965) and 1.624-1.634 (5) Å (Hencher, 1978).

With regard to bond angles, it is known that aromatic ring deformations depend markedly upon the electronic properties of the ring substituents (Domenicano, Vaciago & Coulson, 1975*a,b*; Domenicano, Mazzeo & Vaciago, 1976). In accordance with the general trend in p -substituted anisoles (Di Rienzo, Domenicano, Portalone & Vaciago, 1976), the C(6)-C(8)-C(7') bond angle is slightly smaller than the C(6)-C(7)-C(8') angle. Of particular interest are the internal C-C-C angles at the *ipso* atoms. Their value of 119.3 (2)° is only marginally smaller than the reported substituent constants of 119.9 and 120.2° calculated from a number of reliable data on *para*-disubstituted benzene derivatives with OCH₃ and OH functional groups, respectively (Domenicano, Mazzeo & Vaciago, 1976).

By analogy with *para*-substituted anisoles, the alkoxy substituents give rise to further deformations. Namely, as the oxygen and attached C(α) atom of the alkoxy

Table 4. *Intermolecular contacts (Å)*

Short contacts are arbitrarily defined as being less than the sums of van der Waals radii plus 0.4 Å. The symbols A , \bar{A} and B denote atoms with coordinates x, y, z ; $\bar{x}, \bar{y}, \bar{z}$ and $\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z$, respectively. In this notation $\bar{A}(pqr)$ stands for the fractional coordinates $p - x, q - y, r - z$. E.s.d.'s for the C...C, C...Cl and Cl...Cl distances are about 0.01 Å; no e.s.d.'s can be quoted for intermolecular contacts involving the calculated H atom positions.

A(000)	$\bar{A}(\bar{2}\bar{2}\bar{1})$		A(000)	$\bar{A}(\bar{1}\bar{2}\bar{2})$	
C(7)	C(7)	3.70	C(5)	C(7)	3.97
C(7)	H(7)	3.02	C(6)	C(6)	3.68
H(7)	H(7)	2.62	C(6)	C(8)	3.74
			C(7)	C(8)	3.97
			C(7)	H(51)	2.98
A(000)	$\bar{A}(\bar{1}\bar{0}\bar{1})$				
C(8)	H(31)	3.35	A(000)	$\bar{A}(\bar{1}\bar{2}\bar{1})$	
C(8)	H(41)	3.35	O	H(7)	2.64
			C(4)	H(7)	3.38
A(000)	$\bar{A}(\bar{1}\bar{0}\bar{0})$		C(7)	H(31)	3.22
O	H(41)	2.85	H(41)	H(7)	2.74
C(3)	H(41)	3.39			
C(6)	H(41)	3.00	A(000)	$\bar{A}(\bar{0}\bar{0}\bar{1})$	
C(6)	H(51)	3.11	C(5)	H(31)	3.26
C(7)	H(41)	3.30			
C(8)	H(51)	2.80	A(000)	$\bar{A}(\bar{1}\bar{0}\bar{1})$	
H(32)	H(42)	2.76	Cl	C(5)	3.97
A(000)	$\bar{A}(\bar{0}\bar{0}\bar{1})$		Cl	H(32)	3.34
Cl	H(42)	3.27	Cl	H(52)	3.05
C(1)	C(4)	4.00	C(1)	C(5)	3.89
C(1)	H(42)	3.07	C(1)	H(52)	2.84
C(2)	C(5)	3.87	C(2)	C(8)	3.95
C(2)	H(51)	3.24	C(2)	H(52)	3.28
C(3)	H(51)	3.25	C(2)	H(8)	3.24
H(31)	H(51)	2.41	C(3)	C(8)	3.96
H(31)	H(8)	2.55	H(41)	H(8)	2.61
A(000)	$\bar{A}(\bar{1}\bar{0}\bar{0})$		A(000)	$\bar{B}(\bar{0}\bar{1}\bar{0})$	
C(4)	C(6)	3.77	Cl	Cl	3.76
C(4)	H(32)	3.28	Cl	C(1)	3.34
C(5)	C(6)	3.77	Cl	C(2)	3.47
C(5)	C(8)	3.76			

group lie in the plane of the aromatic ring (Table 3), with a C-O-C angle in the usual range of 117-118° (Di Rienzo, Domenicano, Portalone & Vaciago, 1976), this results in a close approach of C(5) and C(8) [2.84 Å; C(5)...H(8), 2.52 Å] and leads to a strong in-plane bending of the C(6)-O bond. The H...H separations involved in the distortion are in the range 2.28-2.29 Å. The exocyclic bond angles at C(6) are 115.8 (4) and 124.9 (4)°.

The O-C-C side-chain angle is significantly less than the tetrahedral value whereas the C-C-C angles are all significantly greater, lending weight to the argument that bond angles in these systems are dictated by non-bonded interactions.

Of prime importance in influencing the overall packing mode is the difference in steric bulk of the aromatic ($r = 1.7$ Å) and aliphatic ($r = 2.0$ Å) parts of the molecule. Thus, in spite of the short a axis, (I) does

not adopt a layered structure. The inclination of the molecule and the fairly large monoclinic angle are responsible for the few aromatic–aromatic interactions and the more numerous but weaker aromatic–aliphatic interactions. Such an arrangement is consistent with the observed fairly low crystal density and melting point. It is also not surprising to observe that the largest amplitudes of vibration are associated with the terminal atoms of the ring substituents. The shortest intermolecular C···C, C···H, H···H, C···Cl, H···Cl, Cl···Cl and O···H distances are 3.68, 2.80, 2.41, 3.34, 3.05, 3.76 and 2.64 Å, respectively, and conform to normal van der Waals distances (Table 4).

In the majority of juvenile hormone (JH) mimics the carbon skeleton bears either a close resemblance or is identical to that of the natural hormones, where the terpenoid methyl branch occurs every four carbon atoms. The compound in this study strongly departs from the classical structures of JH analogues by the total absence of terpenoid branching and a different functionality at the termini of the aliphatic chains. It has been suggested (Nilles, Zabik, Connin & Schuetz, 1976) that one requirement for biological activity in a JH mimic is the placement of a group with a certain π -electron density 11.5 ± 0.5 Å away from an epoxy oxygen, and conclusions have been drawn about the critical dimensions of a hypothetical receptor site. The finding of the high morphogenetic potency for this mimic cannot be rationalized in terms of its ability to fit this hormone-receptor site.

References

- BETTARINI, F., MASSARDO, P., PICCARDI, P. & LONGONI, A. (1978). Italian Patent Application 24.794 A/78.
- BRYAN, R. F. & FALLON, L. (1975). *J. Chem. Soc. Perkin Trans. 2*, pp. 1175–1180.
- BRYAN, R. F. & FREYBERG, D. P. (1975). *J. Chem. Soc. Perkin Trans. 2*, pp. 1835–1840.
- BRYAN, R. F. & JENKINS, J. J. (1975). *J. Chem. Soc. Perkin Trans. 2*, pp. 1171–1175.
- COLAPIETRO, M. & DOMENICANO, A. (1977). *Acta Cryst. B33*, 2240–2243.
- COTRAIT, M., SY, D. & PTAK, M. (1975). *Acta Cryst. B31*, 1869–1874.
- CRUICKSHANK, D. W. J., PILLING, D. E., BUJOSA, A., LOVELL, F. M. & TRUTER, M. R. (1961). *Computing Methods and the Phase Problem in X-ray Crystal Analysis*, p. 32. Oxford: Pergamon Press.
- DI RIENZO, F., DOMENICANO, A., PORTALONE, G. & VACIAGO, A. (1976). 2nd Yugoslav–Italian Crystallogr. Conf., Dubrovnik, Yugoslavia. Abstr. pp. A102–A104.
- DOMENICANO, A., MAZZEO, P. & VACIAGO, A. (1976). *Tetrahedron Lett.* pp. 1029–1032.
- DOMENICANO, A., VACIAGO, A. & COULSON, C. A. (1975a). *Acta Cryst. B31*, 221–234.
- DOMENICANO, A., VACIAGO, A. & COULSON, C. A. (1975b). *Acta Cryst. B31*, 1630–1641.
- GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst. A27*, 368–376.
- HARK, T. E. M. VAN DEN, HENDRIKS, H. M. & BEURSKENS, P. T. (1974). *Cryst. Struct. Commun. 3*, 703–706.
- HECHT, H. J. & LUGER, P. (1974). *J. Cryst. Mol. Struct. 4*, 383–389.
- HENCHER, J. L. (1978). *The Chemistry of the Carbon–Carbon Triple Bond*, edited by S. PATAI, Part 1, pp. 57–73. New York: John Wiley.
- IMMIRZI, A. (1967). *Ric. Sci. 37*, 743–749.
- JOHNSON, C. K. (1970). ORTEP. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
- KONINGSVELD, H. VAN (1973). *Cryst. Struct. Commun. 2*, 491–494.
- MOORE, F. H. (1963). *Acta Cryst. 16*, 1169–1175.
- NILLES, G. P., ZABIK, M. J., CONNIN, R. V. & SCHUETZ, R. D. (1976). *J. Agric. Food Chem. 24*, 699–708.
- RABINOVICH, D. & SCHMIDT, G. M. J. (1970). *J. Chem. Soc. B*, pp. 6–10.
- ROUSSEAU, M.-P., MEUNIER-PIRET, J., PUTZEYS, J.-P., GERMAIN, G. & VAN MEERSSCHE, M. (1972). *Acta Cryst. B28*, 1720–1724.
- RUBAN, G. & LUGER, P. (1975). *Acta Cryst. B31*, 2658–2662.
- SIMONETTA, M. & GAVEZZOTTI, A. (1978). *The Chemistry of the Carbon–Carbon Triple Bond*, edited by S. PATAI, Part 1, pp. 1–56. New York: John Wiley.
- SLÁMA, K., ROMAŇUK, M. & ŠORM, F. (1974). *Insect Hormones and Bioanalogues*. New York: Springer.
- SLETTEN, J. (1973). *Acta Chem. Scand. 27*, 229–238.
- SLETTEN, J. (1974). *Acta Chem. Scand. Ser. A, 28*, 499–506.
- SLETTEN, J. (1975). *Acta Chem. Scand. Ser. A, 29*, 436–442.
- SUTTON, L. E. (1965). *Tables of Interatomic Distances and Configuration in Molecules and Ions*. Spec. Publ. No. 18. London: The Chemical Society.
- VAND, V., EILAND, P. E. & PEPINSKY, R. (1957). *Acta Cryst. 10*, 303–306.