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Crystal Sructure Analysis Of Dimethyl (Benzo[D][1,3]Dioxol-5-Yl((4-Bromophenyl)Amino)Methyl)Phosphonate

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Abstract: The title dimethyl (benzo[d][1,3]dioxol-5-yl((4-bromophenyl)amino)methyl)phosphonate was obtained in 76% yield from a NaOH catalyzed Claisen–Schmidt condensation reaction between 4-bromophenyl and phosphonate. This product will be used as a key precursor for the development of an alternative route for the total synthesis of the alkaloid Graveoline. Single crystals of the title compound suitable for X-ray diffraction were grown via slow evaporation in ethanol at room temperature. A complete crystallographic study was performed in depth to unequivocally confirm its structure. The crystal structure of the title phosphonate, $C_{16}H_{17}BrNO_5P$, shows two molecules per asymmetric unit (Z = 2) and adopts an E configuration about the C=C double bond. In the title compound, the mean plane of the non-H atoms of the central chalcone fragment C—C(O)—C—C—C is as follow: [root-mean-square (r.m.s.) deviation = 0.0210 Å for A–B and 0.0493 for C–D molecules]. In the crystal, molecules are linked by N–H...O and C–H...O, hydrogen bonds forming S(6), $R^2_2(10)$ and edge-fused $R^2_2(8)$ rings along with chains running parallel to (110).

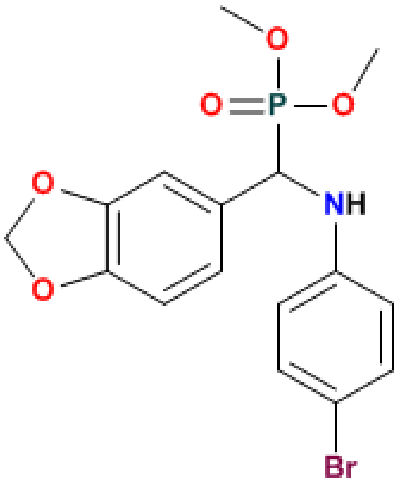
Index Terms - Crystal structure, dioxole, methyl, single crystal X-ray diffraction and phosphinate; T = 295 K; R factor = 0.0523; wR factor = 0.1154; data-to-parameter ratio = 9.08.

I. INTRODUCTION

Five-membered cyclic acetal is a pervasive building block in organic synthesis since it is easily prepared from an aliphatic or an aromatic 1,2-diol. These conversions are often carried out with protection of the contiguous diol [1] to prevent unexpected side reactions or to reduce the polarity of the substrate, especially for carbohydrates. Although masking of the hydroxy groups is a disadvantage in terms of crystallization, due to loss of hydrogen-bond donors, it is expected to stabilize the crystal packing in order to contribute conformational rigidity by forming the cyclic acetal [2]. Tryptophan is one of the nine essential amino acids required by the human body, which cannot be synthesized on its own and must be obtained through diet[3]. It is an aromatic amino acid with an indole side chain, featuring a complex double-ring structure, and serves as a precursor for many bioactive molecules. Tryptophan is relatively rare in nature but plays a crucial role in many protein structures. Its derivatives are diverse and have significant physiological and pharmacological effects in organisms [4]. This paper reports a crystal structure of a tryptophan derivative to assist in the development of new drugs. Thus, chalcones bearing the heterocyclic [5,6]-dioxolo functionality are of particular interest because diverse synthetic and natural compounds containing this functionality in their frameworks have displayed important biological and pharmacological properties [7,8].

II. Experimental

The chemical structure of the compound is shown in Figure 1.The title compound was synthesized using a previously reported procedure [8, 9, 10].



III. Data collection

Data collection: APEX3 (Bruker, 2016)[11]; cell refinement: SAINT (Bruker, 2016); data reduction: SAINT (Bruker, 2016); program(s) used to solve structure: SHELXT (Sheldrick, 2015a)[12]; program(s) used to refine structure: SHELXL2018/3 (Sheldrick, 2015b)[13]; molecular graphics: DIAMOND (Brandenburg & Putz, 2012)[14], PLATON (Spek, 2020)[15]; software used to prepare material for publication: SHELXL2018/3 (Sheldrick, 2015b), PLATON (Spek, 2020) and publCIF (Westrip, 2010)[16].

IV. Refinement

Crystal data, data collection, and structure refinement details are summarized in Table 2. For both compounds, initial structure solution identified positions of all non-H atoms except those of All H-atoms, except for H–N, were positioned at geometrically idealized positions, C–H = 0.9500 Å, C16-H = 0.9900 Å and C32-H = 0.9900 Å and were refined using a riding model approximation with Uiso(H) = 1.2 Ueq(parent atom). H–N atoms were found from the Fourier difference maps, and their coordinates were freely refined. Correctness of the model was confirmed by low residual peaks (0.257) and holes (−0.203 e. Å^{-3}) in the final difference map.

V. Structural Commentary

The title compound crystallizes in triclinic, P-1, with Z = 2. In the molecular structure shown in Figure 2, the central fragments C1–C7(O1)–C8=C9–C10 and C17–C23(O2)–C24=C25–C6 are essentially planar (root-mean-square (r.m.s.) deviation for all non-H atoms = 0.0210 Å and 0.0493 Å respectively) and they form dihedral angles of 1.47(9)◦ and 7.79(15)◦ with the A and C aryl rings, respectively and 4.86(9)◦ and 2.09(15)◦ with the B and D benzodioxol rings, respectively. The amino groups are syn positioned with respect to the carbonyl groups in both molecules. Bond lengths and bond angles in the title molecules are in good agreement with those found in the related compounds of the references [17], with the exception of the C10–C15 and C26–C31 bond lengths. Whereas the title structure exhibits shortened distances of 1.3949(18) and 1.3966(18) Å, respectively, in these compounds, such bond lengths are 1.426(3) and 1.430(3) Å, respectively.

VI. Superamolecular features

The packing arrangement of the title compound can be described by strong intramolecular N–H...O hydrogen bonds and by intermolecular N–H...O and C–H...O hydrogen bonds of medium-strength (see Figure 3 and Table 3), [18]. The molecules unit intertwine to form intra-intermolecular intercalated bonds, generating S(6) and R^2_2 (10) rings [19]. In these interactions, the N2–H3N moiety in the molecule at (x,y,z) acts as a hydrogen-bond donor to the O1 atom of the carbonyl group at (x,y,z) and N1–H1N in the molecule at (x,y,z) acts as a hydrogen-bond donor to the O4 atom of the carbonyl group at (2-x,1-y,1-z). Molecules are connected and they are related by an inversion center, forming a kind of inner ring as seen in Figure 4. One of the molecules unit proceeds to join, via C32–H32...O5 bonds with its twin molecule, configuring dimers with R^2_2(8) rings. Thus, the inner rings are attached to C(18) chains of molecules, forming sheets running parallel to (110)(Figure 5).

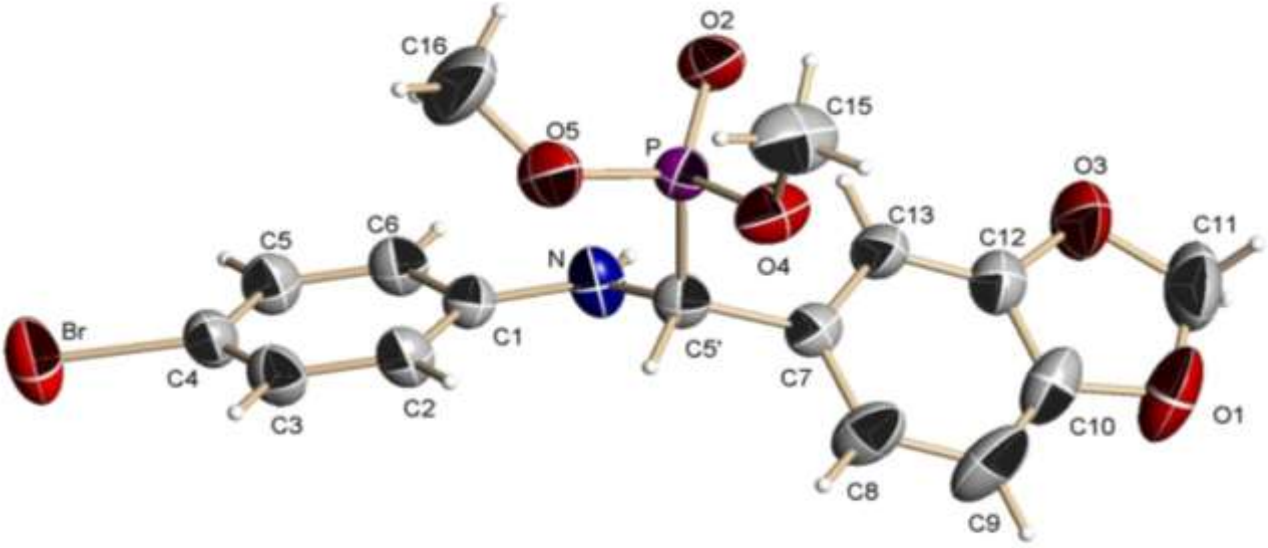


Figure 2 A view of the title compound, showing the atom-labeling scheme. Displacement ellipsoids are plotted at the 50% probability level.

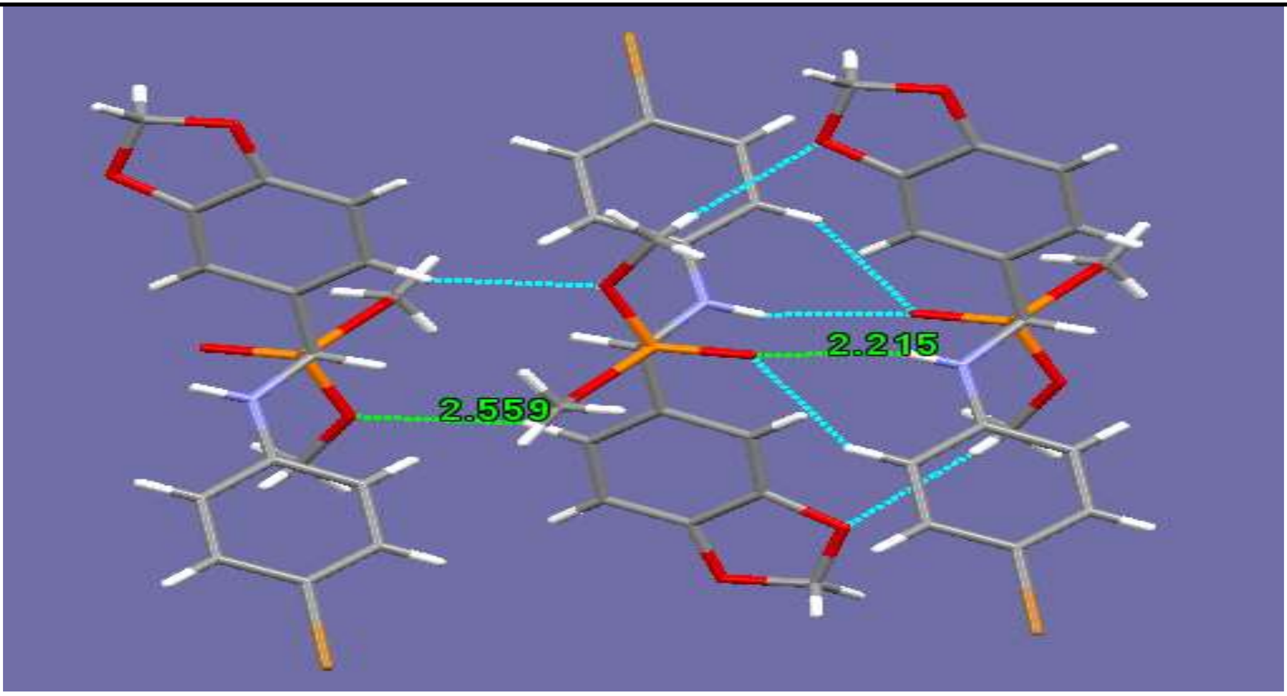


Figure 3 Fragment of a [010] polymeric chain in the crystal structure of the title compound.

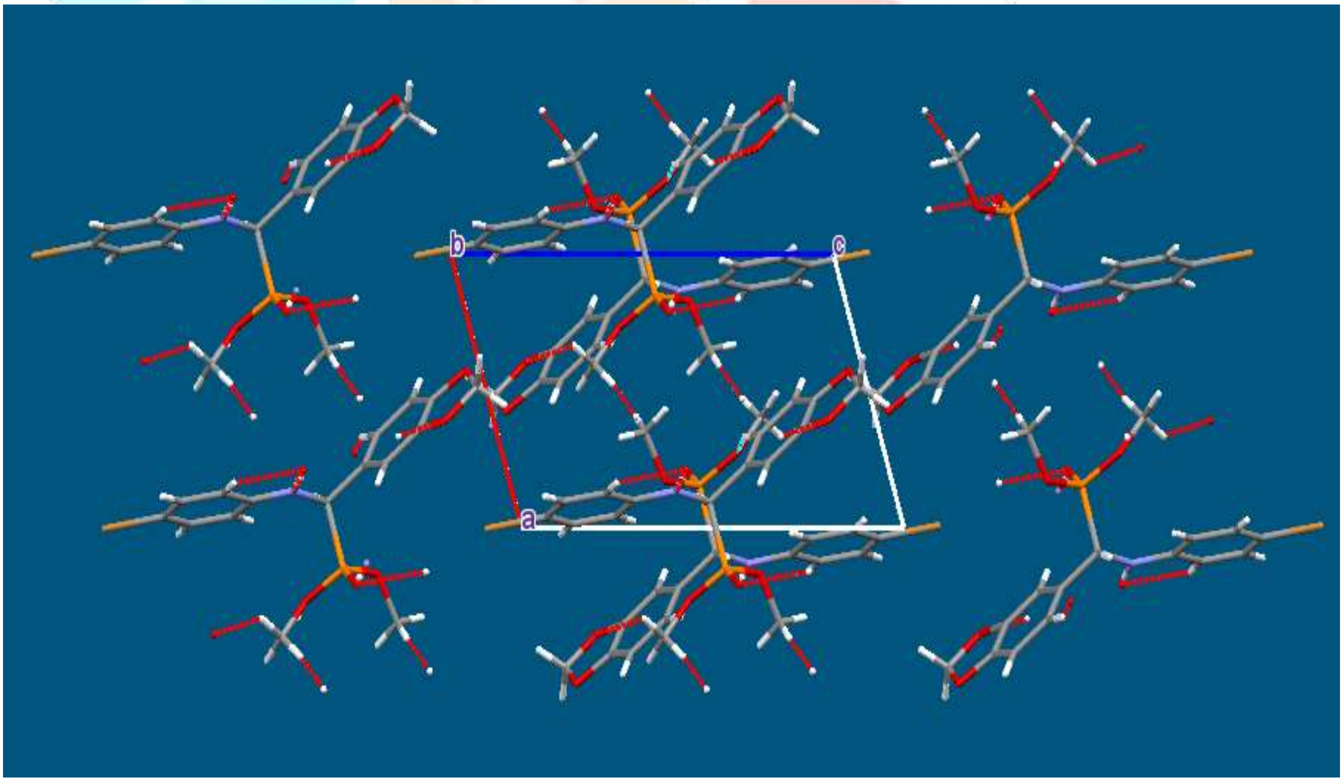


Figure 4 The packing in the crystal of the title complex, viewed along the b axis.

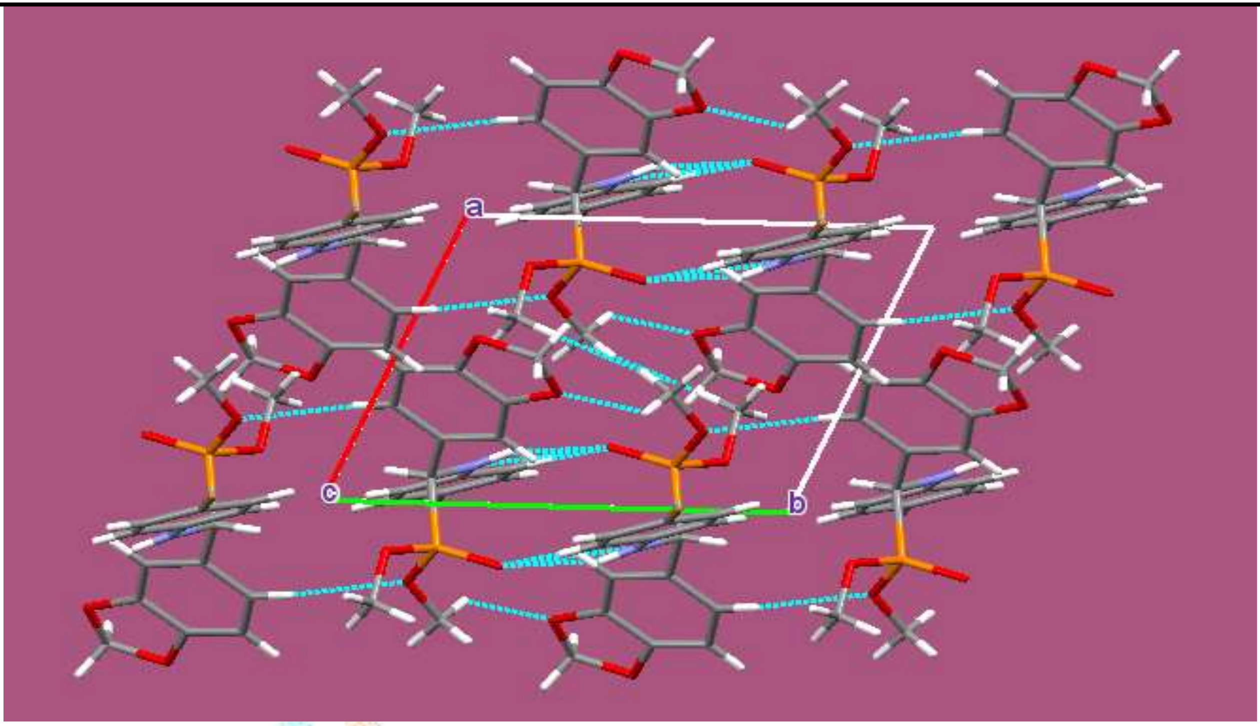


Figure 5 The packing in the crystal of the title complex, viewed along the b axis.

VII. Table: 1

Selected Bond length and Bond angles (Å, °)

Atom	Length(Å)	Atom	Angles(°)
Br-C(4)	1.904(4)	O(2)-P-O(5)	113.52(14)
P-O(2)	1.465(2)	O(2)-P-O(4)	116.48(17)
P-O(5)	1.568(2)	O(5)-P-O(4)	102.91(15)
P-O(4)	1.571(3)	O(2)-P-C(5')	115.13(14)
P-C(5')	1.818(4)	O(5)-P-C(5')	105.33(16)
O(1)-C(10)	1.380(5)	O(4)-P-C(5')	101.89(15)
O(1)-C(11)	1.403(7)	C(10)-O(1)-C(11)	105.2(3)
O(3)-C(12)	1.383(5)	C(12)-O(3)-C(11)	104.6(4)
O(3)-C(11)	1.414(5)	C(15)-O(4)-P	120.3(3)
O(4)-C(15)	1.440(5)	C(16)-O(5)-P	123.9(3)
O(5)-C(16)	1.413(5)	C(1)-N-C(5')	125.5(3)
N-C(1)	1.379(4)	N-C(1)-C(2)	124.7(3)
N-C(5')	1.451(4)	N-C(1)-C(6)	118.1(3)
C(1)-C(2)	1.396(4)	C(2)-C(1)-C(6)	117.2(3)
C(1)-C(6)	1.402(5)	C(3)-C(2)-C(1)	121.2(3)
C(2)-C(3)	1.387(5)	C(3)-C(4)-C(5)	120.6(3)
C(3)-C(4)	1.369(5)	C(3)-C(4)-Br	120.3(2)
C(4)-C(5)	1.380(5)	C(5)-C(4)-Br	119.2(3)
C(5)-C(6)	1.372(5)	C(6)-C(5)-C(4)	119.7(3)

VIII. Table 2

Crystal Data and Details of the Structure Determination

Empirical formula	C16 H17 Br N O5 P
Formula weight	414.19
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 7.9753(3) Å a= 87.671(2)°.
	b = 10.0330(3) Å b= 72.928(2)°.
	c = 12.0946(4) Å g = 68.060(2)°.
Volume	855.51(5) Å3
Z	2
Density (calculated)	1.608 g/cc
Absorption coefficient	2.522 mm-1
F(000)	420
Crystal size	0.48 x 0.27 x 0.15 mm3
Theta range for data collection	1.77 to 25.00°.
Index ranges	-9<=h<=8, -11<=k<=11, -14<=l<=14
Reflections collected	10904
Independent reflections	2889 [R(int) = 0.0313]
Completeness to theta = 25.00°	95.90%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7081 and 0.3761
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2889 / 0 / 220
Goodness-of-fit on F2	1.169
Final R indices [I>2sigma(I)]	R1 = 0.0523, wR2 = 0.1154
R indices (all data)	R1 = 0.0865, wR2 = 0.1247
Extinction coefficient	0.048(4)
Largest diff. peak and hole	0.759 and -0.741 e.Å-3

IX. Table 3

Hydrogen-bond geometry for title Compound (Å ,°).

D-H…A	D-H	H…A	D…A	D-H…A
N1-H1…O2^{i}	0.86	2.22	3.022(4)	156
C6-H6-O2^{i}	0.93	2.54	3.328(4)	142
C8-H8…O5^{ii}	0.93	2.56	3.424(4)	155
C16-H16C…O3^{i}	0.96	2.50	3.285(4)	139

Symmetry codes: i)= 2-x,1-y,1-z
ii) = 2-x,2-y,1-z

X. Acknowledgment

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