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C(4) helices, Br···Br interaction and $R_4^2(10)$ ring in bromoipriflavone

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The title compound, 8-bromo-7-isopropoxyisoflavone (bromoipriflavone), $C_{18}H_{15}O_3Br$, crystallizes in tetragonal crystal system, space group $I4_1/a$ with cell constants $a = 21.396(2)$ Å, $c = 13.588(2)$ Å, $V = 6220.2(14)$ Å^3 and $Z = 16$. Bromoipriflavone is composed of a benzopyranone moiety, a phenyl moiety, an isopropoxy group and a bromine atom. The benzopyranone ring is not coplanar with the phenyl ring with a dihedral angle of 55.1°. The molecules are stacked into a C(4) helices down [001] *via* π–π stacking and hydrogen bonds, the C(4) helices are assembled into three-dimensional network *via* strong Br···Br interactions and synthons $R_4^2(10)$ formed by two tri-centered C—H···O hydrogen bonds, resulting in a distinctive high-symmetry supramolecule. The title compound was also characterized by IR and ^{1}H NMR.

KEY WORDS: Ipriflavone; bromine; crystal structure; supramolecule; hydrogen bonds; π–π stacking.

Introduction

Hydrogen bonds and π–π stacking interactions are an important research content in the supramolecular chemistry and crystal engineering.[1] They play an important role in self-assembly and recognition of aromatic compounds[2,3] as an auxiliary stabilizing short contact.[4–6] Supramolecular synthon is an easy way to describe the short contacts in the crystal structure.[7–9] Ipriflavone, a synthetic isoflavone, is currently used in several countries for prevention and treatment of involutional osteoporosis and has been shown to be effective in reducing bone turnover rate mainly through an inhibition of bone resorption.[10] The title compound, 8-bromo-7-isopropoxyisoflavone, is a derivative of ipriflavone with potential medical applications. In this paper, we synthesized the title compound and its crystal structure was determined by X-ray diffraction analyses. The determination results show that there are a variety of weak but direction-specific intermolecular forces, such as, hydrogen bonds, π–π stacking interactions and Br···Br interactions. π–π Stacking interactions and C—H···O hydrogen bonds link the title compound into a C(4) helices, the C(4) helices assemble into a three-dimensional network *via* strong Br···Br interaction and $R_4^2(10)$ formed by two tri-centered hydrogen bonds at the inversion position, resulting in a distinctive high-symmetry supramolecule. The preparation process of the title compound can be expressed as Scheme 1.

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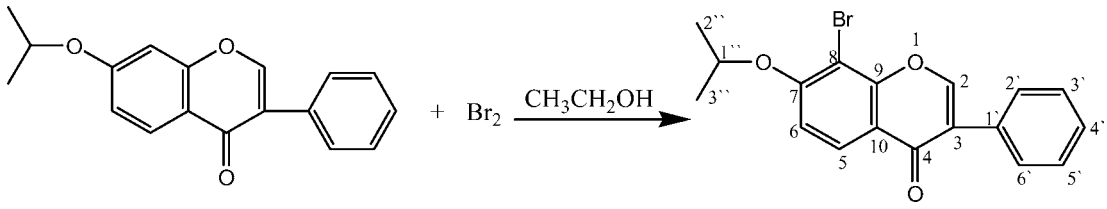

Scheme 1.

Experimental

Synthesis of the title compound

Ipriflavone was purchased from the State-owned Pharmaceutical Company of Wu-Gong. Other chemicals were of analytical reagent grade and were used directly without further purification. The infrared spectra were recorded as KBr pellets on a Nicolet 170SX FT-IR spectrophotometer. The ^{1}H NMR Spectra were recorded on a Bruker Am-300 spectrometer with TMS as internal reference and DMSO-d_6 as solvent. The crystal structure was determined using Siemens P4 Diffractometer instrument.

Ipriflavone (0.5 g) was dissolved in ethanol (100 mL). Bromine (5 mL) was added dropwise to the solution with strongly stirring. The mixture was refluxed for half an hour. After cooling, the mixture was poured into water (100 mL) and colorless precipitation appeared. The precipitate was filtered and washed with water until the pH of the filtrate was 7. After recrystallization from ethanol, the products had melting point of 437 K. Crystals of the title compound suitable for X-ray analysis were obtained from slow evaporation from ethanol after three days at room temperature. IR (KBr) υ: 3432, 2977, 1638, 1597, 1420, 1380, 1271, 1104, 1021, 781, 560 cm^{-1}. The peaks at 1638 and 560 cm^{-1} belong to the —C=O[11] and C–Br [12] vibration of the group in the title compound, respectively. ^{1}H NMR(DMSO-d_6, ppm, 300 MHz): 8.58 (1H, S, H—C_2), 8.08 (1H, d, $J = 7.5$ Hz, H—C_5), 7.58 (2H, d, $J = 9.0$ Hz, H—$C_{2'}$, H—$C_{6'}$), 7.47 (1H, d, $J = 7.5$ Hz, H—$C_{4'}$), 7.42 (2H, dd, $J = 9.0$ Hz, $J = 7.5$ Hz, H—$C_{3'}$, H—$C_{5'}$), 7.35 (1H, d, $J = 7.5$ Hz, H—C_6), 4.93 (1H, m, H—$C_{1''}$), 1.35 (6H, d, $J = 6.0$ Hz, H—$C_{2''}$, H—$C_{3''}$).

X-ray crystal structure determination

The sample selected for investigation had dimensions of 0.58 mm × 0.24 mm × 0.24 mm. The data were collected with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) at room temperature. A total of 3713 reflections were collected to give 3062 independent reflections ($R_{\text{int}} = 0.0412$). The structure was solved using direct methods with SHELXTL software package[13] and refined by full-matrix least-squares techniques. The non-hydrogen atoms were assigned anisotropic displacement parameters in the refinement. The hydrogen atoms were treated using a riding model. The structure was refined on F^2 using SHELX-97.[14] The final R value (on F) was 0.0377. The crystal used for the diffraction study showed no decomposition during data collection. The crystal and refinement data are list in Table 1. Selected bond lengths, bond angles and torsion angles are given in Table 2.

Results and discussion

The title compound, 8-bromo-7-isopropoxyisoflavone, $C_{18}H_{15}O_3Br$, possesses normal geometrical parameters compared with its parent, ipriflavone,[15] in most of the bond distances and bond angles. The title compound is composed of a benzopyranone moiety, a phenyl moiety, an isopropoxy group and a bromine atom. (Fig. 1. The subsequent discussion uses the crystallographic atom naming scheme.) The atoms of benzopyranone ring, including ring A (C10—C15) and ring

Table 1. Crystal Data and Structure Refinement for the Title Compound

Compound	Bromoipriflavone
Empirical formula	$C_{18}H_{15}O_3Br$
CCDC deposit no.	CCDC-244989
Formula weight	359.21
Temperature (K)	298(2)
Wavelength (Å)	0.71073
Crystal system	Tetragonal
Space group	$I4_1/a$
Unit cell dimensions	$a = 21.396(2)$ Å $b = 21.396(2)$ Å $c = 13.588(2)$ Å
Volume, Z	6220.2(14) Å^3, 16
Density (calculated)	1.534 Mg m^{-3}
Absorption coefficient	2.653 mm^{-1}
$F(000)$	2912
Crystal size	0.58 mm × 0.24 mm × 0.24 mm
Theta range for data collection	1.78–25.99°
Limiting indices	$0 \le h \le 26, 0 \le k \le 26,$ $-1 \le l \le 16$
Reflections collected	3713
Independent reflections	3062 [$R_{int} = 0.0412$]
Absorption correction	Empirical
Maximum and minimum transmission	0.9970 and 0.6064
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3062/0/202
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0377$, $wR_2 = 0.0432$
R indices (all data)	$R_1 = 0.1339$, $wR_2 = 0.0473$
Extinction coefficient	0.00205(3)
Largest diff. peak and hole	0.373 and −0.326 eA^{-3}

C (O1/C7─C11), are nearly coplanar with a mean deviation of 0.0191 Å from its best least-square plane. The benzopyranone is not coplanar with the phenyl ring B (C1─C6) with a dihedral angle of 55.1°, which is similar to its parent being 50.0°. The bromine atom is located at atom C12 of ring A, which pushes the isopropyl to the other side compared with its parent indicated by the C16─O3─C13─C14 torsional angle of the title compound being −17.91° and the corresponding torsional angle of ipriflavone being 172.76°. The different orientations of the isopropyl groups between the title compound and its parent are the result of the bromine substituent.

The molecules of the title compound are linked into a three-dimensional network by a variety of weak but direction-specific intermolecular forces, and the formation of this framework is readily analyzed by means of the supramolecular synthon.[8] π–π Stacking interactions link the molecules into C(4) helices along [0 0 1] together with C─H···O hydrogen bonds. Furthermore, the C(4) helices are assembled into a supramolecule *via* the synthon $R_4^2(10)$ built by two tri-centered C─H···O hydrogen bonds at the inversion position and Br···Br interactions (Fig. 2).

In the first submotif, the 4_1 screw axis down [001] generates C(4) helical chains of molecules of the title compound linked by π–π stacking interactions and C─H···O hydrogen bonds (Fig. 2). The adjacent benzopyranone moiety of the molecules of the title compound are not completely parallel with a dihedral angle of 5.1° and stacked with each other viewed down [0 0 1], with a *Cg–Cg#* separation of 3.410 Å [*Cg* is the centroid of the benzopyranone moiety, including

Table 2. Selected Bond Lengths (Å), Bond Angles (°) and Torsion Angles (°)

Br─C(12)	1.895(3)	C(13)─O(3)─C(16)	120.1(3)
O(1)─C(7)	1.360(4)	C(8)─C(7)─O(1)	127.4(4)
O(1)─C(11)	1.369(4)	C(11)─C(12)─Br	121.3(3)
O(2)─C(9)	1.230(4)	C(13)─C(12)─Br	118.7(3)
O(3)─C(13)	1.360(4)		
O(3)─C(16)	1.449(4)	C(5)─C(6)─C(8)─C(7)	−125.4(5)
C(6)─C(8)	1.488(5)	C(5)─C(6)─C(8)─C(9)	55.1(7)
C(7)─C(8)	1.336(4)	O(1)─C(11)─C(12)─Br	1.9(7)
C(8)─C(9)	1.460(4)	C(10)─C(11)─C(12)─Br	−177.2(3)
C(9)─C(10)	1.464(5)	C(16)─O(3)─C(13)─C(14)	−17.9(8)
O(3)─C(13)─C(14)	124.8(4)	C(16)─O(3)─C(13)─C(12)	164.5(5)
O(3)─C(13)─C(12)	116.4(4)	Br─C(12)─C(13)─O(3)	−4.4(6)
C(7)─O(1)─C(11)	116.2(3)	Br─C(12)─C(13)─C(14)	177.9(4)

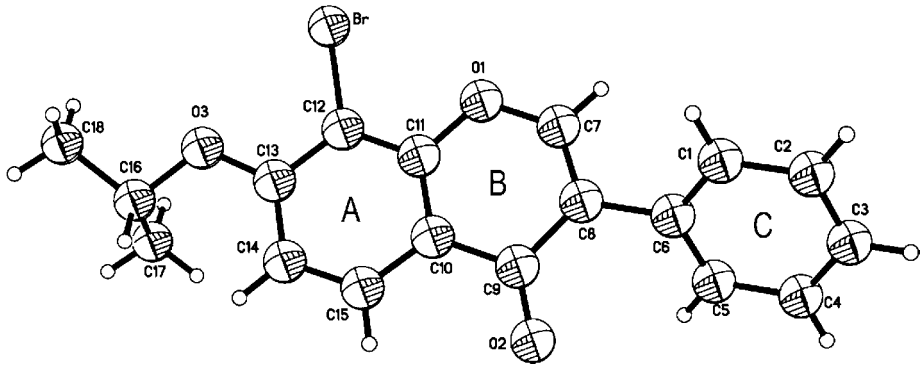

Fig. 1. Molecular structure and atomic numbering for the title compound. Displacement ellipsoids are plotted at the 50% probability level.

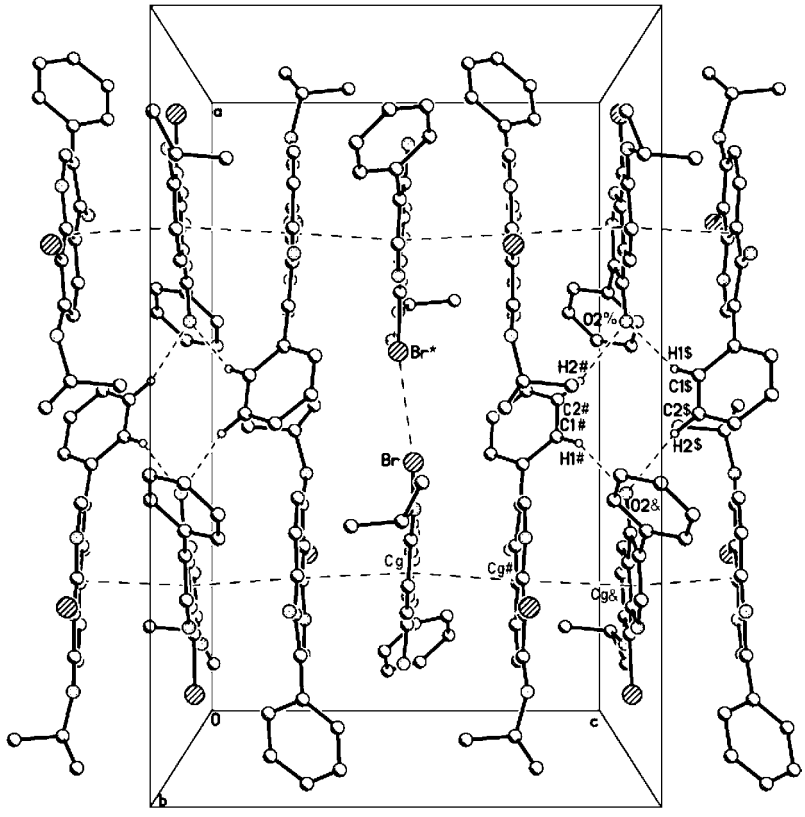

Fig. 2. Part of the crystal structure of the title compound, showing the formation of the C(4) helices, the synthon $R_4^2(10)$, the π–π stacking interactions, the hydrogen bonds and the Br$\cdots$Br interactions. Atoms marked with an asterisk (*), hash (#), ampersand (&), dollar ($), at (@) and percent (%) are at the symmetry positions $(1-x, 1-y, 1-z)$, $(0.75-y, x+0.25, 0.25+z)$, $(0.5-x, 1-y, 0.5+z)$, $(0.25+y, 0.75-x, 1.75-z)$, $(y-0.25, 0.75-x, 0.75+z)$ and $(0.5+x, y, 1.5-z)$, respectively. The horizontal dashed lines indicate the formation of the C(4) helices via the π–π stacking interactions. *Cg* is the centroid of the benzopyranone moiety. For the sake of clarity, some H atoms have been omitted.

atoms O1/C7—C15, symmetry code: (#) $0.75 - y$, $0.25 + x$, $z + 0.25$)]. The corresponding perpendicular distances from *Cg* and *Cg#* to the best least-squares ring planes of the other stacking benzopyranone moieties are 3.408 and 3.387 Å, respectively. The lateral displacement of *Cg#* relative to the normal from the *Cg* best least-square ring plane at *Cg* to the *Cg#* best least-squares ring plane is 0.40 Å. The perpendicular distances and the lateral displacement are agreed with the angle of *Cg*—*Cg#*—*Cg&* being 175.0° [symmetry code: (&) $0.5 - x$, $1 - y$, $z + 0.5$]. The other short contacts forming the helices are extensive hydrogen bonds C1#—H1#···O2& with distance of H1#···O2& being 2.60 Å, C1#···O2& being 3.470(2) Å and bond angle being 155.7°.

Atom C2$ in the molecule acts as hydrogen-bond donor to carbonyl oxygen atom O2& in the molecule [symmetry code: ($) $0.25 + y$, $0.75 - x$, $1.75 - z$], with distances of H2$···O2& being 2.64 Å, C2$···O2& being 3.503(1) Å and bond angle of 154.3°. A tri-centric hydrogen bond is formed by hydrogen bonds C2$—H2$···O2& and C1#—H1#···O2&. Combination of these tri-centered hydrogen bonds at the inversion position generates the second motif $R_4^2(10)$ (Fig. 2).

The last substructure is C12—Br···Br* synthon (Fig. 2). Two bromine atoms link the adjacent C(4) helices at the same layer together with a Br···Br* distance of 3.651 Å and angles of 168.10° [angles of C12—Br···Br* and C12*—Br*···Br are all of 168.10°; symmetry code: (*) $1 - x$, $1 - y$, $1 - z$]. The Br···Br distance is at the normal range compared with the reported criteria (3.40–3.70 Å)[16] of Br···Br interaction, which shown that Br···Br interaction exists in the crystal structure of the title compound.

Supplementary material CCDC-244989 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving. html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk].

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