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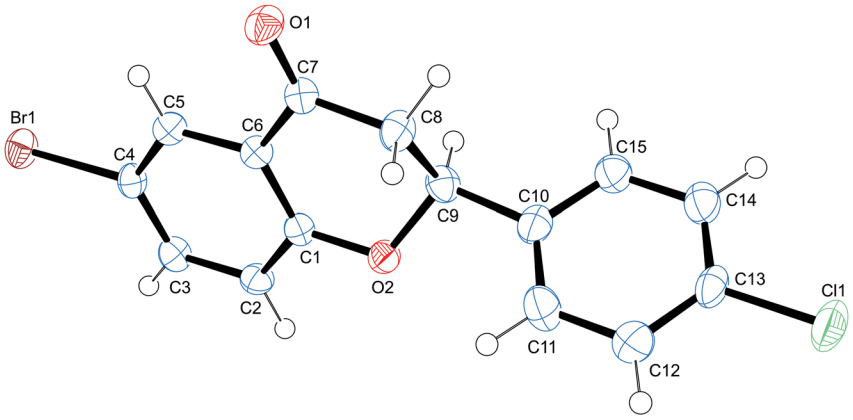
Crystal structure of 6-bromo-2-(4-chlorophenyl) chroman-4-one (6-bromo-4′-chloroflavanone), $C_{15}H_{10}BrClO_2$



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Abstract

$C_{15}H_{10}BrClO_2$ monoclinic $P2_1/c$ (no. 14), a = 9.2173(6) Å, b = 20.7174(14) Å, c = 6.9035(4) Å, β = 99.332(3)°, V = 1300.83(14) Å^3, Z = 4, $R_{gt}(F)$ = 0.0153, w$R_{ref}(F^2)$ = 0.121, T = 173(2) K.

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The crystal structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colorless plate
Size	0.277 × 0.58 × 0.05 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.5 mm^{-1}
Diffractometer, scan mode:	Bruker SMART, φ and ω-scans
θ_{max}, completeness:	25.5°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	45410, 2418, 0.044
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2272
$N(param)_{refined}$:	172
Programs:	Bruker programs [1], WinGX and ORTEP [2], SHELX [3]

Source of material

A stirred mixture of (*E*)-1-(5-bromo-2-hydroxyphenyl)-3-(4-chlorophenyl)prop-2-en-1-one (0.50 g, 1.48 mmol) and piperidine (0.15 g, 1.78 mmol) in ethanol (10 mL) was heated at 80 °C for 2 h and then allowed to cool to RT. The mixture was quenched with an ice-cold water and the resulting precipitate was filtered and recrystallized from ethanol to afford 6-bromo-4′-chloroflavanone as a yellow solid. (0.38 g, 92%), mp.158–159 °C (EtOH) (Lit. [4] 157–159 °C). The crystals for X-ray analysis were prepared by slow evaporation from CH_2Cl_2.

Experimental details

X-ray single crystal data were collected on a Bruker D8 Venture diffractometer with graphite-monochromated Mokα (λ = 0.71073 A) radiation at 173 K using an Oxford Cryostream 600 low-temperature controller. Data reduction was carried out using the program SAINT+, version

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.8044 (4)	0.65976 (19)	0.2707 (5)	0.0227 (8)
C2	0.9437 (4)	0.6376 (2)	0.2510 (6)	0.0260 (8)
H2	0.960269	0.592811	0.234161	0.031*
C3	1.0585 (4)	0.6814 (2)	0.2563 (6)	0.0256 (8)
H3	1.154422	0.666571	0.245674	0.031*
C4	1.0322 (4)	0.74714 (19)	0.2772 (6)	0.0234 (8)
C5	0.8955 (4)	0.76990 (19)	0.2954 (5)	0.0236 (8)
H5	0.879634	0.814846	0.309576	0.028*
C6	0.7791 (4)	0.72597 (19)	0.2930 (5)	0.0221 (8)
C7	0.6304 (4)	0.75000 (19)	0.3059 (6)	0.0251 (8)
C8	0.5147 (5)	0.69829 (19)	0.2947 (7)	0.0295 (9)
H8A	0.466095	0.693426	0.156734	0.035*
H8B	0.439063	0.711713	0.373311	0.035*
C9	0.5786 (4)	0.6334 (2)	0.3701 (6)	0.0281 (9)
H9	0.617842	0.637057	0.513457	0.034*
C10	0.4593 (5)	0.5829 (2)	0.3394 (7)	0.0300 (9)
C11	0.4142 (5)	0.5541 (2)	0.1583 (8)	0.0411 (11)
H11	0.464881	0.563258	0.05218	0.049*
C12	0.2939 (6)	0.5113 (2)	0.1305 (8)	0.0414 (11)
H12	0.262506	0.491296	0.006984	0.05*
C13	0.2231 (5)	0.4994 (2)	0.2885 (7)	0.0331 (10)
C14	0.2665 (5)	0.5277 (2)	0.4690 (7)	0.0358 (10)
H14	0.215414	0.518839	0.574981	0.043*
C15	0.3862 (5)	0.5694 (2)	0.4938 (7)	0.0331 (9)
H15	0.417857	0.58885	0.618176	0.04*
O1	0.6016 (3)	0.80720 (13)	0.3188 (5)	0.0326 (7)
O2	0.6962 (3)	0.61472 (14)	0.2667 (4)	0.0269 (6)
Cl1	0.07143 (13)	0.44768 (6)	0.2577 (2)	0.0490 (4)
Br1	1.19037 (4)	0.80650 (2)	0.28426 (6)	0.03088 (17)

6.02 [1] and empirical absorption corrections were made using SADABS [1]. The structure was solved in the *WinGX* [2] Suite of programs, using intrinsic phasing through *SHELXT* [3] and refined using full-matrix least-squares/difference Fourier techniques on F^2 using *SHELXL-2017* [3]. All hydrogen atoms were placed at idealized positions and refined as riding atoms with isotropic parameters 1.2 or 1.5 times those of their parent atoms. The largest difference density peaks must be attributed to a slight disorder of the bromo substituent distributed over several postions.

Comment

Flavanones (2,3-dihydro-2-phenylchromen-4-ones) are compounds widely distributed in the plant families *Compositae*, *Leguminosae*, *Lamiaceae* and *Rutaceae* [5]. These heterocyclic compounds have attracted significant interest due to their wide range of pharmacological properties including anticancer, antimicrobial, antiproliferative, anti-inflammatory, cardiovascular, antimalarial, antiangiogenic, radical scavenging and hypotensive activities [6]. Their biological properties are closely related to the skeleton and substitution patterns, which continue to motivate research on their synthesis and evaluation of their bioactivity [7]. They are readily accessible *via* acid- or base-mediated cyclization (intramolecular Michael addition) of the corresponding chalcone (1,3-diphenyl-2- propene-1-one) precursors prepared, in turn, *via* acid- or base-mediated Claisen–Schmidt condensation reaction between 2-hydroxyacetophenones and benzaldehyde derivatives [6, 7]. The introduction of one or more halogen atoms into A or B-ring of flavonoids affords the corresponding halogenated derivatives with potential biological activity [8]. Halogen atom/s are very useful to modulate the electronic and steric characteristics of drugs and may also influence the hydrophilic-hydrophobic balance of the molecules [9]. Although the flavanone nucleus does not exert any anxiolytic activity [10], substitution at position 6 of the flavanone nucleus with a bromine atom was found to lead to 6-bromoflavanone [11] or 6-bromoflavone derivatives with elevated anxiolytic properties [12]. Halogenated flavanones, on the other hand, are not only of interest from the medicinal chemistry context [9, 11], their conformations and crystalline structures continue to attract attention to explore non-covalent (intramolecular and intermolecular) interactions, control molecular conformations and improve the physicochemical properties (durability, solubility and bioavailability) of the drug molecules. Based on the diverse biological activities of flavanone derivatives and our longstanding interest in their synthesis and chemical transformation, we decided to synthesize 6-bromo-4′-chloroflavanone and study its geometry in the solid state.

This compound crystallizes in the monoclinic space group $P2_1/c$ containing a single molecule in the asymmetric unit as shown in the Figure. The racemic naturally occurring naringenin (5,7,4′-trihydroxyflavanone/5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one) was also found to crystallize in a monoclinic crystal system in the space group $P2_1/c$ with one molecule in the asymmetric unit [13]. The solid-state structures of the pure *R*- and *S*-enantiomers of naringenin, on the other hand, were previously found to crystallize in the monoclinic space group $P2_1$ with two independent molecules having slightly different geometries [13].

The single crystal structure of the title compound shows the two aromatic rings (A and B) are linked by a pyranone ring (C), which adopts a chair-like conformation in which C9 atom deviates from the plane drawn through the remaining five atoms of this heterocycle with a bond angle, O(2)–C(9)–C(8), of 110.3(3)°. The 2-phenyl ring occupies a quasi-equatorial orientation relative to the flattened portion of the heterocyclic ring and the methine

hydrogen atom is *anti* to one of the methylene hydrogen and gauche to the other. A similar orientation of the 2-phenyl group was observed before in the crystal structures of the racemic and pure enantiomers of naringenin [13]. The *ipso* angle α for substituted benzene derivatives is sensitive to the electron withdrawing inductive effect of the substituent and this observation has previously been rationalized in terms of the hybridization effects of the *ipso* carbon [14]. The presence of bromine atom on the A ring resulted in alternate positive and negative internal angle distortion effect, and the trend is as follows: *ipso* angle, C(5)–C(4)–C(3) = 121.5(4)°; *ortho* angles, C(2)–C(3)–C(4) = 119.8(4)° & C(4)–C(5)–C(6) = 119.2(4)°; *meta* angles, C(3)–C(2)–C(1) = 119.5(4)° and C(1)–C(6)–C(5) = 119.6(4)° and *para* angle, C(2)–C(1)–C(6) = 120.4(4)°. The 2-(4-chlorophenyl) group exhibits a similar trend: ipso angle, C(14)–C(13)–C(12) = 122.3(4)°, *ortho* angles, C(13)–C(12)–C(11) = 117.8(5)° & C(13)–C(14)–C(15) = 119.0(4)°; *meta* angles, C(10)–C(11)–C(12) = 120.6(4)°, C(10)–C(15)–C(14) = 120.5(4)°; and *para* angle, C(15)–C(10)–C(11) = 119.8(4)°.

This contribution, which forms part of our long-standing interest on the geometry and conformation of halogenated oxygen-based heterocycles represents in our view a valuable contribution to the dataset of flavanones of medicinal potential. Since aryl halides represent important intermediates in metal-catalyzed cross-coupling reactions, nucleophilic aromatic substitution reactions and for the generation of free-radical intermediates [15], the reported compound represents a suitable scaffold for further chemical transformation to generate polycarbo-substituted derivatives.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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